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HEBERDEN'S NODES: THE CLINICAL CHARACTERISTIC OF OSTEO-ARTHRITIS OF THE FINGERS

BY

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William Heberden was a prominent English physician of the eighteenth century whose name is associated with several diseases. His most important contribution was read at the Royal College of Physicians on July 21, 1768, and was printed in the Medical Transactions in 1772. This description of angina pectoris was of itself of sufficient importance to assure him of lasting fame. He later published a book[1] in which he described enlargement of the fingers, a condition with which his name has since been uninterruptedly associated. The disease itself is benign and insignificant but references have been made to Heberden's nodes in nearly every study on arthritis which has appeared subsequently. His name has been so intimately associated with arthritis that he has become the patron saint of an organization devoted to the study of joint disease, an association called by his name, the Heberden Society. The present paper, devoted to this form of arthritis named for him, is a review and summary of studies on Heberden's nodes which have previously been reported in detail.

Heberden's original description is so short that it is reprinted in full (Heberden, W., Jun., 1803): *

> "What are those little hard knobs, about the size of a small pea, which are frequently seen upon the fingers, particularly a little below the top, near the joint? They have no connexion with the gout, being found in persons who never had it; they continue for life; and being hardly ever attended with pain or disposed to become sore, are rather unsightly, than inconvenient though they must be some little hindrance to the free use of the fingers."

Heberden obviously had no clear idea of their true nature, but he did dispel for all time the popular fallacy which had prevailed until then that these enlargements were due to gout. Heberden's nodes have been called pathognomonic of, diagnostic of, typical examples of, the commonest manifestation of, and the most benign form of osteo-arthritis. It is now universally understood that they are a particular manifestation of this general disease. Because the lesions are so readily recognized with reasonable certainty, and because they occur with great frequency, the disease lends itself readily to clinical and statistical study. It was thought that important information could easily be obtained from study of this condition which might be applicable to other forms of osteo-arthritis.

Incidence

The present author's interest was originally inspired by his seeing a man with enlarged fingers who stated that four sisters were similarly deformed. The significance of this observation obviously could not be ascertained unless the incidence of Heberden's nodes in the general population were known. It was to answer this particular question that a general survey of the population was undertaken (Stecher, 1940). The hands of nearly 7,000 individuals were examined. These were patients at Cleveland City Hospital and visitors to the dispensaries of two general hospitals as well as the residents in several homes for the aged. Since none of them had been selected because of the condition of their hands it was assumed that, so far as Heberden's nodes were concerned, this group was representative of random sampling of the general population. A separate card made for each individual examined bore the name, age, sex, race, and notes on the condition of the fingers. These cards were sorted into different classifications and were filed alphabetically. Duplication was thus avoided because the card was noted to be a duplicate and was discarded when a subject was seen a second time.

The condition of each deformed finger was described. Three degrees of deformity were recognized. The first was enlargement of the joint big enough to be obvious by inspection. Such enlargement was usually palpable as two round nodules or a dense solid bar across the

* W. Heberden, Senior, died in 1801. The paper from which the quotation has been taken was published by his son, W. Heberden, Junior, in 1803.—Ed.

dorsum of the finger joint at the proximal end of the distal phalanx. As the enlargement became greater it was palpable at the sides of the joint and in extreme cases also on the palmar surface. A second degree of deformity included palmar flexion of the distal joint in addition to enlargement. In general this was seen only in fingers with more than minimal enlargement. The third degree of deformity consisted, in addition to enlargement and flexion, of a lateral deviation from the straight line of the distal phalanx. These designations were found to be reliable indications of three successive stages in the development of Heberden's nodes.

Observation and questioning soon revealed that Heberden's nodes arose in two different ways. Many men were seen even in the second decade of life with moderate enlargement of one finger. Even older men stated that such enlargements arose shortly after and in direct response to trauma. The injury had been painful enough to be vividly remembered and had been sustained in the majority of instances while playing baseball. The deformity had developed within the course of several months but had soon attained a condition which was constant. When once established there had been no progression of the process in the individual finger or extension of the disease to other fingers. Enlargements of the fingers due to injury came to be recognized as such and have been called traumatic Heberden's nodes.

Enlargements due to injuries were occasionally seen on women's fingers. Usually, however, women stated that enlargements of a single finger began gradually without reference to injury, that it slowly increased in size, and that the process gradually extended to other fingers. These were called idiopathic Heberden's nodes to distinguish them from traumatic Heberden's nodes.

In the original survey involving observations on 6,913 individuals the incidence of idiopathic Heberden's nodes in white men rose gradually as age advanced from about 1 per cent. in the third and fourth decades to 18·2 per cent. in the ninth decade. This was different from the findings in white women. These showed 15·5, 24·7, and 29·4 per cent. in the seventh to the ninth decades. Because the apparent tendency to level off at a maximum incidence in old age seen in white females was entirely lacking in males, a resurvey was made of the condition in higher age groups (Stecher and Hersh, 1944). Based on observations in 151 white men and 184 white women of 70 years of age or over, the findings in women were about the same as in the original survey but the incidence was much lower in white men, only about 3 per cent. affected being found. Increased experience with the condition over a period of years served to eliminate more accurately the cases of traumatic nodes which had previously been included. Table 1 as now published is adapted from the original study. The revised figures for white males in the eight and ninth decades have been added in a footnote.

The study led to several general conclusions.

TABLE 1

INCIDENCE OF TRAUMATIC AND IDIOPATHIC HEBERDEN'S NODES IN 6,913 SUBJECTS

Age group	20–29	30–39	40–49	50–59	60–69	70–79	80–89
2,233 *white men*							
Number examined	324	306	446	439	353	203	44
Traumatic nodes	7·1%	8·0%	9·2%	15·5%	23·2%	23·6%	11·4%
Idiopathic nodes	1·5%	1·0%	2·2%	3·6%	5·4%	8·4% *	18·2% *
2,187 white women							
Number examined	500	498	512	306	207	125	34
Traumatic nodes	0·2%	3·2%	5·7%	12·7%	12·1%	16·8%	5·9%
Idiopathic nodes	0·0%	0·4%	1·0%	2·6%	15·5%	24·7%	29·4%
846 *negro men*							
Number examined	184	249	191	131	75	16	
Traumatic nodes	8·2%	6·0%	10·0%	9·9%	14·7%	12·5%	
Idiopathic nodes	0·5%	0·4%	0·5%	3·1%	6·7%	6·3%	
1,117 *negro women*							
Number examined	330	346	255	124	48	12	2
Traumatic nodes	0·0%	2·3%	2·7%	4·0%	14·6%	16·7%	50·0%
Idiopathic nodes	0·0%	0·3%	0·0%	0·0%	2·1%	8·3%	0·0%
530 *white physicians*							
Number examined	104	147	165	73	34	7	
Traumatic nodes	1·9%	4·8%	4·8%	11·0%	11·8%	14·3%	
Idiopathic nodes	0·0%	0·0%	0·0%	2·7%	2·9%	0·0%	

* In the resurvey, 4 of 129 men aged 70 to 79—or 3·2 per cent.—and 1 of 24 men aged 80 to 89—or 4·2 per cent.—had idiopathic Heberden's nodes.

The incidence of both types of Heberden's nodes tends to increase with age. The incidence of traumatic nodes is higher in men than in women, is higher in manual workers than in physicians, and is higher in white manual workers than in negroes. The differences in incidences of traumatic nodes between various groups of white people seem to depend upon difference in exposure of the fingers to trauma. The incidence of idiopathic nodes is universally low before the age of sixty, after which it increases very rapidly in white women. About one-third of white women become affected if they live long enough. The condition never attains a high proportion in men.

Heredity

When the incidence of Heberden's nodes for each sex and age group was known, the influence of heredity was investigated (Stecher, 1941). All the available relatives of 68 affected people were examined. Of 67 mothers of these people, 21 were said to have had Heberden's nodes. Of 129 sisters of affected women 33 were said to have Heberden's nodes. By classifying these relatives by age in decades and multiplying the number found in each decade with incidence for the particular classification, the number expected affected if this group had been normal was computed. It was found that the mothers of affected women were affected twice as often, and the sisters of the affected women were affected three times as often, as would have been expected in the normal population on the basis of chance alone. The details of these computations as they appeared in the original study are shown in Table 2.

In a control series chosen to resemble the study series as closely as possible in age and sex distribution, the sisters of non-arthritic index cases were found to be affected about as frequently as was expected in the general population. The mothers were all reported to have been unaffected.

The probability of multiple family involvement was computed in three families. This was done by multiplying the incidences for all the affected brothers and sisters. It was found that such combinations were not to be expected by chance alone more often than once in 190, once in 4,500,000 and once in 10,000,000 families. Photographs of the available affected members in the last family are shown in Fig. 1. They consisted of a brother aged 59 and sisters aged 60, 58, and 50 years when seen. An additional affected sister died at the age of fifty-six. The probability for individual involvement, based on sex and age incidence as shown in Table 1, is 2·6 per cent., 2·6 per cent., 2·6 per cent., 3·6 per cent., and 15·5 per cent. The probability for such involvement combined in one family by chance alone is $0{\cdot}026 \times 0{\cdot}026 \times 0{\cdot}026 \times 0{\cdot}036 \times 0{\cdot}155$ equals 0·000000098 or one in about 10,000,000 times. It seemed reasonable to conclude that heredity played an important role in the production of these cases of Heberden's nodes in families.

Mechanism of Inheritance

The mechanism of inheritance was then investigated (Stecher and Hersh, 1944). Analysis was made of the pedigrees of 74 affected persons involving a total of 127 men and 215 women. Of the 215 women, 108, or one-half, were found to be affected, a proportion suggesting immediately that the trait was inherited as a simple dominant. In a simple dominant one parent is expected to be affected. In this series an affected parent, invariably the mother, was found in only 25 of the 74 families. In view of the rarity of the condition in men it was assumed that the trait though dominant in women might be recessive in men. The affected parent in some cases might be the apparently normal father. Since nearly

TABLE 2

OCCURRENCE OF HEBERDEN'S NODES IN RELATIVES OF AFFECTED PERSONS: 68 FAMILIES

Age groups	Age incidence	In 67 mothers			In 129 sisters		
		Total mothers	Expected affected	Recorded affected	Total sisters	Expected affected	Recorded affected
20–29	0·000	2	0·000	0	6	0·000	0
30–39	0·004	4	0·016	0	16	0·064	1
40–49	0·010	3	0·030	0	17	0·170	3
50–59	0·026	9	0·234	0	39	1·014	10
60–69	0·155	19	2·945	8	31	4·805	14
70–79 .. .	0·347	16	3·952	9	11	2·717	2
80	0·294	14	3·823	4	9	2·646	3
Totals ..		67	11·000	21	129	11·416	33

one-third of the population had been found to be heterozygous for Heberden's nodes, one-third of the fathers were expected to be genotypically normal in all families in addition to the obviously affected mothers.

In genetic studies on human material the attainment of Mendelian ratios is prevented by two particularly important factors, small family size and lack of penetrance. Correction for small family size by Hogben's method was applied to two different groups (Hogben, 1933). In one group of 29 families with known maternal involvement and suspected but unrecognized involvement in one third of the fathers, 53 of 95 daughters were observed affected. This compared favourably with the 54·9 expected affected with 1 : 1 ratio. In 35 families with apparently normal maternal inheritance and suspected paternal inheritance, 46 of 96 daughters were observed affected compared to 57·7 expected affected.

Correction for lack of penetrance was then made in the following manner. The age of onset of Heberden's nodes had been satisfactorily identified in 95 women. Of these 95 women the median age of onset was 48 years. At 54 years of age, three-quarters of these 95 women had developed Heberden's nodes. The family groups were sorted according to age. The incidence found between 30 and 48 years was doubled. The incidence found between 49 and 54 years was corrected by multiplying by four-thirds, and the incidence of those 55 or over was not altered. These corrections gave the number finally expected affected.

When these corrections had been made for small family size and for incomplete penetrance, the 29 families with observed maternal inheritance and suspected inheritance from one-third of the fathers as well, showed that 66 of 95 daughters, or 70 per cent., are finally expected affected. This is a ratio of over 2 affected to 1 normal rather than the usual 1 : 1 ratio expected in a simple dominant with one parent affected. The unrecognized involvement in one-third of the fathers accounts for the excessive ratio. In 35 families without suspected maternal inheritance and with paternal inheritance alone 53·6 of 96 daughters, or 56 per cent. are finally expected affected. This approximates very closely the theoretical 1 : 1 ratio expected with one affected parent.

On the assumption that the trait is recessive in men, sons would be affected only in response to double inheritance. With such a heritage a 3 : 1 ratio would be expected among daughters. In 4 such families of known double inheritance, as indicated by the presence of affected sons, 8 of 11 daughters were affected—a close approximation to theoretical expectancy in such circumstances.

In spite of an apparent lack of agreement with Mendelian ratios the analysis showed, on the basis of numerical tests, that these data support the hypothesis of a genetic mechanism of idiopathic Heberden's nodes involving a single autosomal gene, sex-influenced, dominant in females and recessive in males.

Osteo-arthritis of Other Joints

The association of Heberden's nodes with osteo-arthritis in other parts of the body was investigated (Stecher, 1946*b*). Of 94 women with Heberden's nodes, 12 were found to have osteo-arthritis of other joints. In 11 patients this involved the knee, in one patient the hip. It was never severe enough to incapacitate the patient, but it did cause inconvenience and discomfort in most instances. Deformity was not marked, but limitation of motion and crepitus was noted in all the affected knees. Several of the patients had a decided limp but none required a cane or crutch. All took acetylsalicylic acid and many had resorted at one time or another to physical therapy, particularly diathermy and massage. Aside from the 12 patients mentioned above, 19 others complained of arthritis or rheumatism. They had transient stiffness, occasional soreness, and questionable swelling, and had used acetylsalicylic acid for relief. Their symptoms were intermittent, but no objective signs warranting a diagnosis of osteo-arthritis were found. These patients were not investigated as a routine by *x*-ray examination.

All knees were tested for crepitus by palpation during motion. Crepitus was noted in 34, or 36 per cent., of the cases. The patient was often unaware of this condition. Crepitus cannot be considered normal. It does not of itself warrant a diagnosis of osteo-arthritis. It is not necessarily a forerunner of future joint disability. The significance of crepitus in these cases is not clear.

In the control series of about 109 women of about the same age distribution, 3 had osteo-arthritis of a knee diagnosed because of pain, limitation of motion, and deformity. Crepitus was noted in only 25, or 23 per cent., of the women, compared to 36 per cent. in the study series.

The marked preponderance of osteo-arthritis in patients with Heberden's nodes compared with those in the control series is apparent. The occurrence of joint disease with objective evidence of pathologic change explaining the symptoms in 12 of 94 affected women compared with 2 of 109 control cases is obviously too great to be explained by chance alone.

Relation to Hypertension

A study of blood pressure was made comparing 112 women with Heberden's nodes and 92 women of the control series (Stecher, 1946*a*). Both groups were of similar age distribution. The control series was otherwise chosen at random. It was found that average blood pressures for each age decade were about the same in each group. After combining both series into one group, no significant association between Heberden's nodes and hypertension could be demonstrated. The coefficient of

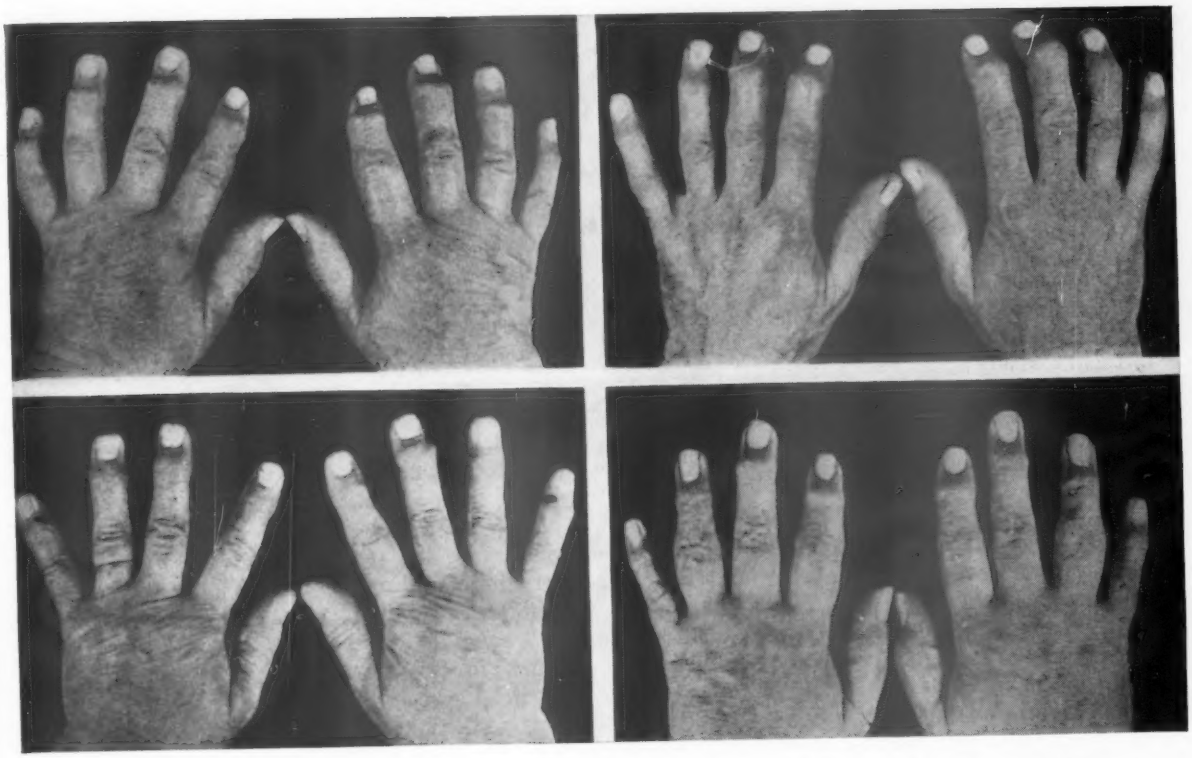

FIG. 1.—The hands of the four living of the five members of one family affected with Heberden's nodes.

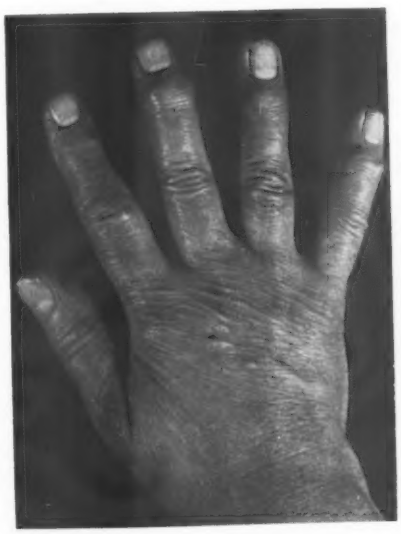

FIG. 2.—Right hand of a 51-year-old woman, showing marked variation in the degree of development of Heberden's nodes.

FIG. 3. — Antero-posterior radiographs show normal index and ring fingers and deformity of the middle finger. The little finger shows mushrooming of the ends of the bones, with spur formation.

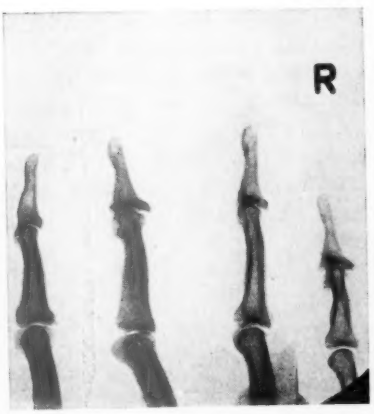

FIG. 4.—Lateral radiographs of the fingers shown in Fig. 2 show marked spur formation arising from the attachments of the flexor and extensor tendons.

association was +0·25. In a further series of 82 women with hypertension Heberden's nodes were found only as frequently as was to be expected in the normal population. It was concluded from these findings and from a review of the literature that Heberden's nodes or osteo-arthritis of the fingers does not differ in relation to hypertension from osteo-arthritis of other joints.

Relation to Obesity

The relationship between Heberden's nodes and obesity was then studied, the same control being relied upon (Stecher, 1946*a*). No association was found in this series between Heberden's nodes and obesity, despite the fact that a strong positive association has been noted in the literature between osteo-arthritis and obesity. In this respect, Heberden's nodes differ widely from osteo-arthritis of other joints.

Relation to the Menopause

The relationship of the menopause to Heberden's nodes was then investigated (Stecher and Beard, unpublished). Ninety-nine women with Heberden's nodes who had passed the menopause were studied. The age of onset of Heberden's nodes in these women ranged from 33 to 65 years. The median age was 49·8 years and the average age was 46·8 ± 6·8 years. The age of the menopause in these women averaged 48·6 ± 5·25 years. This was about the same as found for the control group in which the menopause averaged 48·9 ± 4·9 years and quite similar to the results in the study of 1,000 English women in which the menopause averaged 46·4 ± 3·9 years (Report of the Sub-committee of the Council of Medical Women's Federation, 1933). The menopausal history in women with Heberden's nodes did not appear to be unusual. The average difference in age between the menopause and the onset of Heberden's nodes was 4·92 ± 4·0 years. The menopause preceded the onset of Heberden's nodes in 44 instances and the menopause followed the onset in 45 instances. Both events occurred in the same year in 10 instances. If the time interval between these two events is computed in the same direction, assigning a positive value when the menopause precedes the onset and a negative value when it follows the onset of Heberden's nodes, the average difference is +0·72 ± 6·3 years. A wide dispersion of these values was found, the menopause occurring from 15 years before to 20 years after the onset of Heberden's nodes.

Despite the wide dispersion, close association of the menopause to the onset was observed in many cases. In 10 instances both events occurred in the same year. In 44 instances, or in nearly half the women, the menopause and the onset of Heberden's nodes occurred within 3 years of each other. The correlation coefficient for the two events was found to be + 0·46 ± 0·08 a figure which is significant. Although the correlation coefficient is significant and nearly half the patients with Heberden's nodes noted a close relationship in point of time between these two events, the rest of the patients noted no such association.

Only one-third of all women are genotypically susceptible to Heberden's nodes. The majority of them, therefore, will escape the defect under every circumstance. Of the susceptible one-third who get Heberden's nodes, only about one-half develop the disease in association with the menopause.

The mechanism by which the menopause influences the production of Heberden's nodes is not clear, but two possibilities are discussed. The menopause stimulates the production of gonadotropic hormone and probably also of growth-promoting hormone by the pituitary gland. Animal experiments are reviewed showing that growth-promoting hormone in mature animals stimulates proliferation of joint cartilage and adjacent bone. This occurs in acromegaly, but the pathological changes in acromegaly are quite different from those in Heberden's nodes. Furthermore, the menopause is characterized by numerous manifestations of abnormal vasomotor regulation, particularly of the extremities. Impairment of circulation to bone is thought to be a major factor in the production of osteo-arthritis. Regardless of the mechanism involved, the menopause is thought to be only a contributing factor and not a determinative one in the aetiology of Heberden's nodes.

Radiological Appearance of Heberden's Nodes

A detailed study of the clinical and radiological appearance of Heberden's nodes indicate that marked changes in the fingers may be observed in radiographs taken in lateral views which are not suspected in conventional postero-anterior exposures (Stecher and Hauser, 1948). Lateral views reveal large exostoses arising from the proximal ends of the distal phalanges in the attachments of the extensor and flexor tendons. These may become quite large, almost enclosing the entire distal end of the middle phalanx. Such pronounced abnormalities are seen even in fingers which show only moderate changes in routine postero-anterior radiographs. It was also observed that marked enlargements of the fingers due to soft-tissue swelling occur before bony changes are revealed. Some attempt was made by means of serial photographs and radiographs to indicate the rate with which Heberden's nodes develop. Contrary to popular opinion, involvement of proximal interphalangeal joints with

osteo-arthritis was noted in 40 per cent. of the cases studied.

The features described are illustrated in the example shown. A photograph of the dorsum of the right hand (Fig. 2) shows a normal index finger and a nearly normal ring finger, a marked enlargement and flexion deformity without deviation of the middle finger, and a similar but less severe deformity of the little finger. Antero-posterior radiographs (Fig. 3) show normal index and ring fingers, and deformity of the middle finger which does not seem nearly as severe as the photographs would suggest. The little finger shows mushrooming of the ends of the bones with spurs. There is a knob-like enlargement of the distal end of the middle phalanx, with foam-like distortion of the trabeculae. The lateral radiographs (Fig. 4) show marked spur formation, not revealed in antero-posterior projection, arising from the attachments of the flexor and extensor tendons.

Neurotrophic Influences

Heberden's nodes rarely affect all fingers, and when they do so the fingers are likely to show appreciable variations in the degree of involvement. This characteristic is particularly noticeable during the early stages of the disease before the deformities are completely developed to their final and permanent shape. The local conditions which determine these differences in otherwise normal fingers are not recognizable. One influence which acts as a local determinant in allowing the development of Heberden's nodes has been identified. This is a normal and intact nerve supply. Defective nerve supply prevents the development of Heberden's nodes.

Numerous examples have been described of patients with Heberden's nodes on one hand but without nodes on the other hand, having several fingers the seat of trophic disturbances following a nerve injury. Such failure of development of Heberden's nodes was seen in denervation from severance of a peripheral nerve, due to atrophy of the hand following anterior poliomyelitis and to paralysis following apoplexy. One patient with well-developed Heberden's nodes bilaterally had a slight apparent decrease in their size on one hand 15 months after that hand was partly paralysed due to cerebral haemorrhage. This apparent decrease in size was the result of soft-tissue shrinkage because radiographs showed no change in the size of the finger bones. Nerve injuries or lesions of the central nervous system affect the vasomotor mechanisms in the paralysed areas, causing increased blood circulation to the bone and leading to osteoporosis. Heberden's nodes apparently do not develop in the presence of osteoporosis.

Other Clinical Features

Heberden's nodes exhibit considerable variation in their size, shape, and general appearances. In some instances " the little hard knobs " are apparent as the first manifestation of the disorder and remain as a characteristic feature of the deformity. In other instances there are no " little hard knobs " but a subcutaneous bar-shaped enlargement across the dorsum of the joint. In certain instances there is a general enlargement of the joint in all diameters. Flexion deformity may be slight or absent but is usually apparent, and it becomes marked if there is considerable enlargement. Deviation is the rule when enlargement is marked, but even then may be entirely absent.

Heberden's nodes may begin as a small, round, fluctuant, tender mass, a little to one side of the dorsum of the joint. This fluctuant mass may become as large or even slightly larger than any bony deformity of Heberden's nodes itself, but it usually decreases in size as the fluctuant nature of the enlargement changes to bony hardness. This explains how patients occasionally notice that their finger enlargements have become smaller. If these fluctuant masses are evacuated they yield a colourless, thick, jelly-like amorphous mass.

Fluctuant masses such as these have been described by Gross, who called them degenerative myxomatous cysts of the synovia (Gross, 1937). He stated that surgical removal was useless because the cysts recur repeatedly. He believed that *x*-ray radiation abolished them permanently. We have had no experience with *x*-ray radiation in this condition. We have seen three such cysts removed surgically. In each instance the patient subsequently developed Heberden's nodes at the site of the cyst. The largest nodes in each case were invariably on the finger which had been treated surgically.

Women of the working class invariably attribute their Heberden's nodes to the influence of hard manual labour or to the frequent exposure of their hands to water. That these opinions are not warranted is indicated by the fact that these deformities are equally common among women who have never done hard work or who have never had their hands in water except for personal bathing. The author knows of no evidence indicating that the production of idiopathic Heberden's nodes is influenced in the least by climate, occupation, diet, housing, environment, habits of living, the general state of nutrition, or conditions of general health.

Conclusions

Investigation of the natural history of Heberden's nodes reported here seems to justify certain con-

clusions. It is revealed that two conditions are necessary for the development of idiopathic Heberden's nodes. These include, first, the hereditary constitution or the genotype. This might be considered a theoretical supposition because the non-susceptible genotype is never recognizable; the susceptible genotype is recognizable only after the subject develops Heberden's nodes. The study in heredity indicates that about one-third of white women, 32·6 per cent.—29·9 per cent. as heterozygotes and 2·7 per cent. homozygotes—and 2·7 per cent. of white men as homozygotes are genotypically susceptible. The second condition necessary for the development of Heberden's nodes is an intact and normally functioning nerve supply to the hand and fingers.

Hereditary susceptibility and normal nerve supply may be considered as determinative factors.

Other factors which are not determinative but which seem to be secondary factors include race, age, and menopause. It is possible that each of these factors controls or modifies a separate condition which must be fulfilled to allow Heberden's nodes to develop. It is possible that each of these factors controls or modifies the same condition which must be fulfilled to allow Heberden's nodes to develop.

Although Heberden's nodes are a manifestation of osteo-arthritis they constitute a particular form of this disease with characteristics specific for this disease. Other forms of osteo-arthritis no doubt have particular characteristics specific for them. If they also were studied and the characteristics of different kinds of osteo-arthritis were compared, it seems that the fundamental nature of this general disease might be brought nearer to recognition.

Fig. 1 is reprinted with permission of the Editor of the *American Journal of Medical Sciences*. Figs. 2, 3, and 4 are reprinted with permission of the Editor of the *American Journal of Roentgenology and Radium Therapy*. Table 1 was constructed from material previously published (Stecher, 1940; Stecher and Hersh, 1944). Table 2 is taken from a previous study (Stecher, 1941).

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Nodules d'Heberden

Conclusions

Les recherches ci-dessus sur la nature des nodules d'Heberden semblent justifier certaines conclusions. Elles ont révélé que deux conditions sont nécessaires au développement des nodules idiopathiques d'Heberden. La première est la constitution héréditaire ou le génotype. Cette hypothèse pourrait être considérée comme purement théorique car on ne peut jamais identifier le génotype des individus non sensibles, et le génotype sensible ne peut être affirmé qu'après l'apparition des nodules d'Heberden. L'étude génétique indique que, pour les femmes de race blanche, un tiers environ, 32·6 pour cent à 29·9 pour cent comme hétérozygotes et 2·7 pour cent comme homozygotes, et 2·7 pour cent des hommes blancs comme homozygotes, sont génétiquement sensibles. La deuxième condition nécessaire au développement des nodules d'Heberden est l'innervation normale de la main et des doigts.

On peut considérer la sensibilité héréditaire et une innervation normale comme les facteurs déterminants.

D'autres facteurs moins importants sont la race et l'âge de l'individu et la ménopause. Il est possible que chacun de ces facteurs contrôle ou modifie un état déterminé qui doit exister pour permettre le développement des nodules d'Heberden. Il est également possible que chacun de ces facteurs détermine un même état qui permet le développement des nodules d'Heberden.

Bien que les nodules d'Heberden soient des manifestations d'ostéo-arthrite, ils constituent une forme particulière de cette maladie avec des caractéristiques spécifiques. Il est probable que d'autres formes d'ostéo-arthrites ont aussi des caractéristiques particuliéres qui leur sont propres. Il semble que si elles étaient étudiées également et que l'on compare les caractéristiques des différentes sortes d'ostéo-arthrite, on pourrait arriver à élucider la nature même de cette maladie générale.

PAIN IN THE ARM: A REVIEW

BY

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No one will deny the common occurrence of pain in the arm, nor the frequency with which the diagnosis of brachial neuritis was formerly made in such cases. Nevertheless, the pathology of brachial neuritis has not yet been described convincingly, and in recent years attention has been focused upon certain other common syndromes, the study of their well-defined morbid anatomy leaving little doubt that they are responsible for a very large proportion of cases of pain in the arm. We now believe that brachial interstitial neuritis is a comparatively uncommon condition and that this diagnosis should be made only rarely, when all other causes of brachial pain have been excluded.

The accompanying Table gives a fairly comprehensive list of the causes of the symptom in question, arranged roughly according to the site of the lesion, but only five syndromes will be discussed in detail, namely: the root symptoms and signs of spondylitis; prolapse of a cervical intervertebral disc; compression at the thoracic outlet; brachial neuritis; referred pain.

Examination and Interpretation of Physical Signs

Before proceeding, it may be well to reconsider certain elementary principles. A complete history and physical examination are essential, and should include the whole nervous system, the joints and the muscles, in which signs of weakness, wasting, or localized tender areas should be noted. In those cases where there is evidence of nerve involvement, it must be determined whether the lesion is in the cord, the nerve roots, the brachial plexus, or the peripheral nerves, and an accurate knowledge of the skin areas and muscles supplied by the roots and peripheral nerves is essential for this purpose. But when considering sensory loss due to root lesions it should be remembered that there is considerable overlap of the dermatomes supplied by each spinal root, and thus sensory loss can only be expected in the area supplied *solely* by the affected root. Proximally this area may be too narrow to map out, but pain from a root lesion will be felt throughout the entire area supplied by that root, even in the narrow proximal area just mentioned, and may overlap other dermatomes. Paraesthesiae from root lesions are similarly distributed, but tend to be felt more in the distal part of the limb.

In a complete lesion of a peripheral nerve the area of sensory loss to light touch is greater than that to pin-prick, whereas in a complete root lesion the opposite is found. Progressive compression of a nerve without total interruption of conductivity also produces a greater area of loss to pin-prick than to light touch; this is responsible for the dissociated anaesthesia which may be found in cases of cervical rib.

It is comparatively easy to differentiate the muscle weakness or wasting in a complete root or peripheral nerve lesion. But in progressive compression certain muscles will be more affected than others and confusion will arise. Further, the nerve supply of most muscles receives components from several roots, a single root lesion rarely causing complete muscle paralysis.

In conditions producing referred pain, there will be, of course, no signs of organic neurological disturbance, but wasting of the small hand muscles occurs in many cases of rheumatoid arthritis and may easily be mistaken for the effects of a nerve lesion.

Nerve Symptoms and Signs in Spondylitis

The neurological symptoms of vertebral rheumatism have been admirably reviewed by Buckley (1945). The two most important conditions giving rise to root involvement are ankylosing spondylitis and osteo-arthritis.

In the former the symptoms occur in the early stages, when there is epidural and peri-radicular exudate. Later, fibrosis determines the permanency of the residual signs; they are not due to bony narrowing of the intervertebral foramina and are much less common when the spine has become fixed.

TABLE

CENTRAL OR CEREBRAL	thalamic pain
AT CORD LEVEL	spinal tumour syringomyelia haematomyelia localized arachnoiditis tabes dorsalis meningo-vascular syphilis poliomyelitis subacute combined degeneration
AT INTER-VERTEBRAL FORAMEN	*disease of nerve root or root ganglion:* radiculitis herpes zoster neurofibroma *disease of vertebrae:* fracture caries osteomyelitis Paget's disease new growth displaced discs spondylitis, ankylosing „ osteo-arthritic „ rheumatoid
AT THORACIC OUTLET	cervical rib abnormal first rib costo-clavicular compression normal first rib pressure scalenus syndrome acroparaesthesiae glands and tumours
IN THE ARM	*pressure and trauma:* fracture occupational neuritis trauma in ulnar groove pressure on median nerve in carpal tunnel pressure in palm causalgia *neuritis:* polyneuritis toxic neuritis (e.g., arsenic, alcohol) interstitial neuritis paralytic brachial neuritis *referred pain:* from visceral disease (e.g., angina pectoris from skeletal disease (bones, joints, tendons, muscles, " myalgic lesions ", " fibrositis ") *vascular disease:* thrombosis embolism Raynaud's phenomenon

Sciatic pain is well known as an early symptom of the disease, and is often considered to be referred from an affected sacro-iliac joint; but if there are signs of a root lesion, such as sensory loss or an absent ankle jerk, pressure on a nerve root in the lumbo-sacral region must be held responsible.

In osteo-arthritis root symptoms and signs are more common. Some cases of so-called " brachial interstitial neuritis " are due to this cause. It may also produce occipital headache when the first, second, and third cervical roots are involved; such cases are often wrongly diagnosed as primary " fibrositis ". We shall see later how tender nodules may be associated with nerve-root irritation in this and other syndromes, so adding to the difficulty of diagnosis. Signs of nerve-root irritation frequently arise before demonstrable osteophytes are present, being produced while the osteophytes are forming. Soft-tissue changes, and not pressure from new bone, are thus probably responsible. On the other hand, symptoms may not occur until osteo-arthritis has been present for years. In this case it frequently happens that the roots irritated arise from that part of the vertebral column which shows least evidence of osteophyte formation and which is still comparatively mobile; a certain degree of mobility is usually necessary to cause root irritation. Various factors may produce an exacerbation of symptoms by causing soft-tissue reaction and swelling. These are strain or minor trauma, chill or damp, an intercurrent infection, or a septic focus.

Symptoms and Signs.—All the symptoms and signs of root pressure may be encountered, namely pain and paraesthesiae of root distribution, muscle weakness and wasting, and alteration in reflexes. Fibrillation sometimes occurs. The neck movements are usually painful and limited in varying degrees, but, as already pointed out, the neck may actually move best around those joints which are in relation to the affected roots.

Differential Diagnosis.—Although the sixth cervical root, being the largest, is that most frequently affected, osteo-arthritis tends to involve several roots. A uniradicular lesion should always raise the suspicion of a prolapsed disc. The pain from root pressure in osteo-arthritis is not so severe as that in cord or vertebral neoplasm. It is relieved by rest, and aggravated by movement. As the local soft-tissue reaction subsides, so does the pain; this also tends to occur the more nearly the neck becomes fixed. In neoplasm, both symptoms and signs progress relentlessly, and there may be signs of pressure on the cord which, of course, do not occur in osteo-arthritis.

The three-quarter profile radiograph of the cervical spine should always be taken and may reveal obstruction of the intervertebral foramina. But osteo-arthritic lipping may occur without nerve-root involvement, and its presence is no proof that the symptoms are due to this cause: the appearance is common in the sixth and seventh cervical vertebrae in prolapse of the sixth intervertebral disc.

Treatment.—In ankylosing spondylitis treatment is on the usual lines for this disease. In osteo-arthritis, superficial heat is useful, but deep heat, such as short-wave diathermy, may cause swelling of the soft tissues

FIG. 2

FIG. 1.—Radiograph from a case of suspected protrusion of the fifth and sixth cervical discs. The corresponding intervertebral spaces are narrowed anteriorly.

FIG. 1

FIG. 2.—Bilatera cervical ribs, showing asymmetry of the thoracic outlets. Symptoms were present only on the right side.

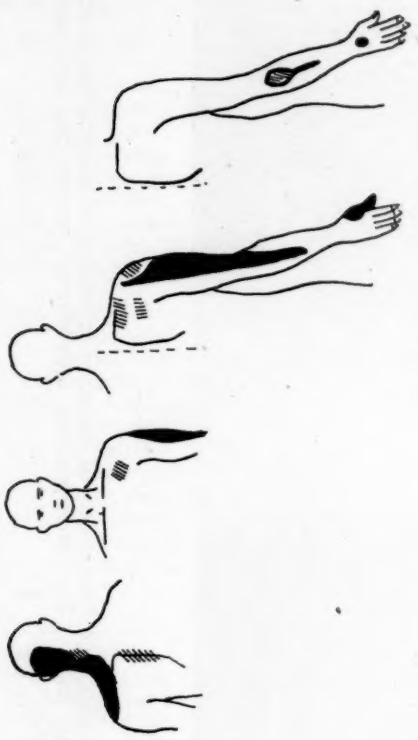

FIG. 4

FIG. 3.—Partial thenar atrophy in a case of thoracic outlet syndrome (no cervical rib seen in the radiograph).

FIG. 4.—"Common sites of myalgic areas (hatching) and referred pain (dark shading)." (After Kellgren.)

FIG. 3

and so increase the symptoms. The same applies to deep *x*-ray therapy. Neck exercises and movements should be given, and gentle massage to the neck muscles is useful. Manipulation by an orthopaedic surgeon can be carried out in some cases. The paretic muscles should receive the same treatment as in other root or peripheral nerve lesions.

Herniation of a Cervical Intervertebral Disc

Rupture of a cervical intervertebral disc may cause spinal-cord compression with associated root signs at the level of protrusion. But root compression without cord involvement can occur, giving rise solely to root symptoms and signs in the arm (Semmes and Murphy, 1943; Spurling and Scoville, 1944; Elliott and Kremer, 1945). This is usually the case when the protrusion is laterally placed, more medial lesions producing the complete syndrome. The first cervical nerve leaves the cord between the occiput and the atlas, where there is no disc, so that a lesion of the sixth disc (that between the sixth and seventh cervical vertebrae) will press on the seventh root. As the roots leave the cord at a fairly wide angle, each root passes over one disc only, in contradistinction to the condition existing in the lumbar region. Unless there are several disc protrusions, the symptoms are therefore uniradicular. Most often the seventh cervical root is affected, the sixth and fifth roots less frequently.

Pain is the chief complaint and is of a dull, gnawing character (Elliott and Kremer), often spreading from the supraspinous region to the posterior axillary fold and lateral shoulder region; thence down the outer side of the arm to the second and third digits in a lesion of the seventh cervical and to the thumb if the sixth cervical is involved. In four left-sided cases described by Semmes and Murphy, the pain was referred to the praecordium, as well as to the left arm, and, not unnaturally, in some of these coronary occlusion was at first suspected. Paraesthesiae are often present and may be severe; they are chiefly felt peripherally. Coughing, sneezing, and flexion of the head towards the side of the lesion sometimes aggravates the pain, which is often worse at night owing to flexion of the neck.

Physical Signs (in Lesions of the Seventh Cervical).—Pressure on the forehead from behind, with the neck bent towards the side of lesion, may reproduce pain, but perhaps not till after the pressure has been applied for several minutes (Spurling's sign). Weakness and wasting of the triceps and extensors of the forearm may occur, but is usually slight. The triceps commonly feels flabby (Elliott and Kremer, 1945), and the triceps jerk may be diminished or absent. Sensory loss is found chiefly in the index finger, but may involve the middle finger to a less degree. (It is important to remember that in most textbooks the index finger is not considered to lie in the seventh cervical dermatome.) There is often limitation of neck movements with spasm of the neck and shoulder muscles. Tenderness may be found over the exit of the affected root and also at various trigger points, in, for example, the upper fibres of trapezius, and pectoralis major; also in the triceps and the extensor muscles of the forearm. Electromyography of these points shows a constant increased irritability, and procaine injection often relieves pain. The significance of these findings will be discussed later.

Special Examinations.—As in lumbar disc lesions, the cerebrospinal fluid may show slightly increased protein, but the dynamics of the fluid are usually normal. Incidentally, lumbar puncture sometimes causes a severe exacerbation of pain. Radiographs may show narrowing of the affected disc space (Fig. 1), with lipping anteriorly and in the region of the intervertebral foramen. This latter change can only be seen in oblique views. Opinions differ regarding the assistance given by contrast media, but it may be said that pantopaque is the only one which is of any use. With this substance Elliott and Kremer showed filling defects opposite the affected discs and lack of filling of the corresponding root sheath.

Treatment.—Owing to the presence of the spinal cord the operation for removal of a disc in the cervical spine presents far more difficulty than in the lumbar region. Fortunately conservative treatment is very often successful and should always be tried first in cases where there is only root compression. The patient should be allowed to find the most comfortable position for his neck, and his pillows should be adjusted to retain it in this position. In more severe cases head traction by harness is needed. If these measures fail, laminectomy, with removal of the offending disc, must be performed.

Compression at the Thoracic Outlet

(Excluding glands and tumours)

According to Walshe and others (1944) the conditions causing compression at the thoracic outlet may be divided into two categories, namely: those in which there is some structural abnormality of the outlet, and those in which it is normal. The following are included:

1. Cervical ribs } abnormal and asymmetrical outlets (Fig. 2)
2. Abnormal first ribs }

3. Normal first rib pressure } normal outlets
4. Costo-clavicular compression }
5. Scalenus syndrome }

Associated with the asymmetrical outlets there may be other developmental abnormalities, such as scoliosis, wedge-shaped vertebrae, extra half laminae, or the Klippel-Feil syndrome of fusion of several cervical vertebrae.

Symptoms and Signs.—These may be of three kinds occurring separately or together, namely: vascular, sympathetic, or somatic nervous.

(a) VASCULAR

(1) *Arterial:* due to disturbance of circulation of the brachial or axillary arteries. They consist of: recurrent coldness, cyanosis, pallor, and tingling in the affected arm; symptoms due to a patent aneurysmal dilatation of the artery (pulsation and bruit above the clavicle) ischaemic phenomena, and occasionally embolism from completely or partly occluded aneurysm.

(2) *Venous:* due to compression of the subclavian vein.

The arterial symptoms were once thought to be due to kinking of the artery over the abnormal rib; then to interference with the sympathetic supply to the vessel. This view has been criticized by Walshe and his colleagues, who consider that the vessel can be nipped between the clavicle and the uppermost rib. In a recent article, Telford and Mottershead (1947) show that this does not occur when the shoulder is depressed, but that it does happen in a small number of cases of abnormal ribs when the shoulder is braced back or the arm is fully elevated. They point out that in depression of the shoulder the clavicle is carried forward and the costo-clavicular gap is actually widened. They further state that the phenomenon of alteration of the pulse is due to compression of the artery distal to the clavicle by the two heads of the median nerve, and therefore has nothing to do with costo-clavicular compression. Clearly there is no one cause to which vascular symptoms can invariably be ascribed in these various syndromes. The variations from the normal are large, and so are the mechanisms which may be brought into play.

(b) SYMPATHETIC

These signs, which can include Horner's syndrome on the affected side, are considered by Walshe to be due to interference with the stellate ganglion, through traction on the subclavian artery or the formation of scar tissue in the vicinity.

(c) SOMATIC NERVOUS

(1) *Thenar type.*—There are pain, paraesthesiae, and sometimes objective sensory loss on the ball of the thumb and the radial side of the forearm. Kinnier Wilson (1940) has described the typical partial thenar atrophy which occurs, involving the upper and outer half of the area, due to wasting of those muscles supplied by the median nerve, that is, abductor pollicis brevis, opponens pollicis, and half of flexor pollicis brevis (Fig. 3).

(2) *Ulnar type.*—Here pain and sensory loss occurs on the ulnar aspect of the hand and forearm, with wasting of the interossei and adductor pollicis; there may be an appearance of the *main en griffe*. Occasionally there is weakness of serratus anticus and winging of the scapula.

In all these syndromes it must be stressed that symptoms are due to a variety of causes operating together or separately. They have been conveniently grouped by Walshe and his co-authors as:

1. Anatomical (the variations of the thoracic outlet).
2. Pathological (soft-tissue changes, such as scar formation, following constant respiratory movement).
3. Physiological (dropping of the shoulder girdle from atonic muscles, the carrying of heavy weights, or trauma).

In cases ascribed to normal first rib pressure or the "scalenus anticus syndrome", rib, clavicle, post fixation of the plexus, and sagging of the shoulder girdle, all play their part in causing symptoms, and sometimes pressure of scalenus anticus or medius is also concerned. This is probably due to the position of the neurovascular bundle in relation to the insertion of the scalene muscles and not to the fact that they are in spasm. Such a condition is unlikely to occur if the rest of the neighbouring muscles are atonic. As Le Vay (1947) has pointed out, there is good evidence that in certain cases the clavicle may compress the neurovascular bundle against the knife-like edge of the scalenus medius.

Treatment.—Unless there are fairly marked signs of nerve damage, conservative treatment may be tried first. Massage to the muscles with "shoulder-shrugging" exercises should be carried out in an attempt to raise the shoulder girdle. If there is progressive weakness and wasting of the hand muscles, operation must be considered. This should always be of an exploratory nature, and the surgeon must be prepared to deal with the particular mechanism of compression which he discovers.

Walshe (1945) has recently drawn attention to the common syndrome of acroparaesthesiae in middle-aged and elderly women. Here sagging of the shoulder girdle due to fatigue and atonic musculature causes paraesthesiae, pain, and circulatory disturbance in both upper limbs, without gross physical signs. The condition has become common in the war and post-war years when elderly women, unaccustomed to these activities, have been forced to stand in queues and to carry shopping baskets for long periods. The treatment is rest and support of the arms in slings, with massage and exercises to restore tone to the muscles of the shoulder girdle.

Brachial Neuritis

Pain in the arm, together with muscle weakness, wasting, and sensory loss, may occur as a symptom of all the varieties of polyneuritis, in the neuritis of diabetes, and in that due to alcohol or arsenic. It is not intended to discuss these further. The diagnosis of interstitial brachial neuritis was once one of the commonest in medicine, but with our present knowledge of the morbid anatomy of the cervical region and shoulder girdle, and recent researches into referred pain and the nature of fibrositis, it is safe to say that pain in the arm should now only be ascribed to interstitial neuritis when all other possible causes have been excluded. Opportunities for examination of nerves in so-called interstitial neuritis have been very few. Denny-Brown (1933) examined the sciatic nerve in one of his patients who died following oxygen injection for sciatica and found exudate under the perineurium of the individual nerve fibres. More recently Holmes and Sworn (1946) have found evidence of

what they call "radiculitis" in certain cases of negative exploration for herniated lumbar discs. There was swelling of the affected nerve root, or adhesions around it, but of course histological examination was not possible.

There is, however, a very definite entity that has come into prominence during the war years, which is variously known as "localized neuritis of the shoulder girdle" (Spillane, 1943), "acute brachial radiculitis" (Aldren Turner, 1944), or "paralytic brachial neuritis" (Martin and Elkington, 1946). The essential features are: pain in the shoulder girdle and down the outer side of the arm, followed at varying intervals of hours, days, or weeks, by muscle weakness and wasting, usually of the shoulder girdle and upper arm. The signs may suggest involvement of (1) a single peripheral nerve (2) several peripheral nerves, or (3) nerve roots. In some cases the signs are bilateral. The serratus anticus is frequently involved, producing a winged scapula, the well-known cases of long thoracic palsy being probably examples of this syndrome. Sensory loss is found in the appropriate areas when nerves such as the circumflex or musculo-cutaneous are involved, and tendon reflexes may be lost. Constitutional and febrile disturbances are usually absent. A peculiar feature is that patients in hospital for unrelated conditions are frequently affected. The cerebrospinal fluid is normal as a rule, but occasionally there is a slight excess of protein. This helps to distinguish the condition from poliomyelitis, with which it is liable to be confused. The prognosis is variable, many cases remaining paralysed for long periods or even permanently. The treatment is that of other forms of flaccid paralysis.

There are various forms of compression neuritis and occupation neuritis. For example the ulnar nerve may suffer repeated trauma in the ulnar groove at the elbow or be affected by chronic periostitis in this region. Recently Russell Brain and others (1947) have described the syndrome of spontaneous compression of both median nerves in the carpal tunnel. It should not be forgotten that various forms of organic nerve involvement may be heralded by an occupation neurosis such as writer's cramp.

Referred Pain and Fibrositis

Disease of the shoulder joint, its ligaments, bursae, and the muscles and tendons in the vicinity, can cause pain referred to the arm. Space does not permit me to consider the conditions fully, but I would mention periarthritis of the shoulder, subacromial bursitis, and tendinitis, which are often considered together as Duplay's syndrome.

Much interesting work has recently been done on referred muscle pain, and new light has been thrown on the aetiology of fibrositis, but this can only be mentioned briefly. Kellgren in 1938 showed that muscle pain may be referred in a distribution which follows a segmental pattern and that tenderness is associated with the referred pain. In the light of this observation, he examined certain cases of fibrositis or myalgia and was able, by study of the areas of referred pain, to localize the points from which this pain arose. Novocaine injection of the primary myalgic area abolished both local and referred pain. By studying his diagrams it will be seen how such cases must often have been mistaken for interstitial neuritis, tenderness of muscle having been confused with that of nerve (Fig. 4).

Elliott (1944) has drawn attention to myalgic areas in the gluteal region in cases of sciatica due to the proved disc lesions and in the extensor muscles of the arm where cervical nerve roots are involved. He examined these with the electromyograph, and found spontaneous motor activity therein. He considers that this is due to involuntary spasm of small groups of muscle fibres caused by irritation of the motor root more centrally. He further suggests that localized spasm can be induced through a reflex path which involves the anterior horn cells, and that the source of excitation may be in or outside the actual nerve root.

Kelly (1945) believes that these myalgic lesions may sometimes arise from visceral disease, for example in the kidney or heart. The visceral disease can cause: (a) reflex (referred) muscle spasm and deep tenderness; (b) radiation of pain impulses to the site of election in muscle, which then takes on a degree of self-sufficiency and produces (c) a myalgic lesion with the usual secondary effects. By analogy, he postulates a reflex theory for the production of post-traumatic myalgic lesions and of fibrositis in general. This is a fascinating hypothesis, and if proved will explain much that was unsatisfactory in the aetiology of fibrositis. It is fairly easy to conceive a myalgic area of muscle spasm arising as a result of any of the following conditions, which we know may be associated with fibrositis: (1) trauma; (2) local cold or damp; (3) root lesions from spinal osteo-arthritis or discs; (4) generalized muscle pains of influenza or subacute rheumatism; (5) fibro-fatty herniations (Copeman's nodes).

The primary myalgic area is usually the most tender, though the patient will often complain most of the pain in the area of reference. It is important to remember that novocaine injections should be made into the primary area. For example, a myalgic lesion in the supraspinatus causes pain to radiate into the deltoid in which a tender area may be felt. Injection in the supraspinatus will frequently relieve the pain, whereas if the deltoid is injected the pain

will be aggravated. The same applies to pain in the forearm and hand arising from a primary lesion in the extensor muscles near their proximal attachment.

Myalgic lesions around the shoulder girdle are frequently associated with gross limitation of movement of the shoulder joint (frozen shoulder) due to periarthritis. This may require manipulation under an anaesthetic. It is interesting to speculate which arose first, the myalgic lesion, or the periarthritis.

Concluding Remarks

In concluding this review I would emphasize the following most important point. The discovery of some abnormality which is, by itself, capable of producing pain in the arm, is no proof that it is the lesion causing symptoms in this particular case. For example, myalgic or "fibrositic" spots can give referred pain, but may themselves be secondary to root lesions from other causes. Osteo-arthritic lipping is often present in cases with a disc lesion. Cervical ribs and abnormal thoracic outlets are frequently associated with other pathological conditions, notably syringomyelia. One of the cases described by Russell Brain and others (1947) deserves particular mention here. Compression of both median nerves in the carpal tunnels was diagnosed and successfully treated by operation, despite the fact that radiographs revealed bilateral cervical ribs, a Klippel-Feil deformity of the cervical spine, and a Sprengel shoulder. The original paper should be consulted for full details, as there can be few better examples of the value of painstaking examination, and the correct interpretation of physical signs, without which the clinician will have little success in the diagnosis and treatment of the causes of pain in the arm.

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Douleur du Bras

RÉSUMÉ

Un tableau donne une liste complète des causes de la douleur du bras classées *grosso modo* en fonction du siège de la lésion. Cinq syndromes sont discutés en détail: les symptomes et les manifestations radiculaires de la spondylite; la hernie d'un disque intervertébral; la compression juxta-thoracique; la névrite brachiale; la douleur irradiante. L'examen et l'interprétation des signes physiques sont discutés. On insiste sur le fait que même dans le cas de la découverte d'une anomalie capable en elle-même de provoquer une douleur dans le bras, il n'est pas prouvé que ce soit cette anomalie qui cause les symptomes dans le cas étudié.

THE HEBERDEN SOCIETY

A General Meeting of the Society was held at 11, Chandos Street, London, W.1, on Oct. 17 and 18, 1947. Summaries of the papers read and the discussions are given below.

SPONDYLITIS

C. W. BUCKLEY

At the time of the world war 1914–18 ankylosing spondylitis, then generally known under the name given to it by Pierre Marie, " spondylose rhizomélique ", was regarded as a rare disease. Now few will deny that it is much more common, though some prefer to say that this is due only to its more frequent recognition. Two questions should be considered in this connexion, first, what are the earliest diagnostic evidences of ankylosing spondylitis? and secondly, does not the term rheumatoid spondylitis obscure the issue as to whether the disease in question is or is not a form of rheumatoid arthritis? which I and not a few others hold to be " not proven ". I therefore propose to devote my remarks mainly to these two points.

The late Gilbert Scott, who had a wide experience of the radiological aspects of the disease, believed, I think, that it began invariably in the sacro-iliac joints, and he coined the term sacro-iliitis for its earliest manifestations. His views have been widely accepted and the evidence to the contrary has often been overlooked. Study of antero-posterior views in radiological examination certainly give some support, but oblique views very often seem to tell a different story.

Borak[1] has studied the radiological appearances in 200 cases spread over a period of more than twenty years in several clinics both in Vienna and in the U.S.A., and has arrived at conclusions which are at variance with those generally held and which seem to me to demand careful study with a view to their confirmation or refutation. He holds that the primary change in the sacro-iliac region is a para-sacro-iliac osteosclerosis, evidenced at first by increased density which passes gradually into complete loss of structural detail. The area of condensation is irregular but sharply defined, and usually symmetrical on the two sides, spreading along the margin of the joints but limited to the iliac bones. The sacrum is involved only in the later stages of the disease and even then infrequently. The contour and width of the sacro-iliac joints, he asserts, are not affected at this stage. He emphasizes Scott's observation that pain is absent from these joints in the most active stage of the disease, in contrast to the local pain and tenderness in sacro-iliac strain or tuberculosis affecting the joints. He finds the earliest evidence of joint affection, as distinct from bone, in the apophyseal joints of the vertebrae, shown by rarefaction of the articular processes and blurring of the outlines of the facets, with pain on pressure or movement, though he agrees that the stage of para-sacro-iliac osteosclerosis passes early into ankylosis of the sacro-iliac joints. Decalcification sets in as the disease advances in the spine as well as the pelvis, passing to complete demineralization around the sacro-iliac joints as well as elsewhere, and obliteration of the joint space goes on to complete osseous ankylosis. These views are based on serial observations extended over many years, largely on oblique views. His other conclusions are interesting and worthy of further study, but time will not permit of further reference.

Freund, at a recent necropsy of a case dying from other causes, found, among other features, that connective tissue spread from the bone marrow as well as the capsule into the joint space, attacking the cartilage in this way: an observation which I found interesting since I have always believed that the disease begins in the bones and not in the joint tissues, thus supporting the opinion of Pierre Marie and Leri that it is an infective or toxic osteopathy.

Oppenheimer[2], in an important paper, stated that in a number of cases the sacro-iliac joints were normal both on clinical and radiological examination and in these cases the apophyseal joint lesion was confined to the thoracic and cervical vertebrae.

More recently Kuhns of Boston and Douglas Taylor of Toronto have stated in a discussion on spondylitis that in their opinion sacro-iliitis is not invariably the precursor of spondylitis.

Sashin in 1930 reported his findings in 257 post-mortem examinations. These changes are, he says, progressive and increase both in extent and intensity with the age of the individual. He emphasizes that

[1] *Radiology*, 1946, 47, 128.

[2] *Amer. J. Roentgen.*, 1943, 49, 49.

they were very common and were uniformly found after the third decade and were more frequent and extensive in the male. He gives the percentage of bony ankylosis in males as 57 per cent. between the ages of 40 and 49 and 60 per cent. between 50 and 59; the corresponding percentages in women were 0 and 14 respectively. These figures are important in respect of the question whether sacro-iliac changes are indicative of spondylitis and especially in view of the sex distribution.

Golding has summarized the problem in a series of questions: (1) What percentage of sacro-iliac infections progress to spinal involvement? (2) Are there two types of sacro-iliac joint lesion, one of which precedes spondylitis and the other not? (3) What is the explanation of the fact that some patients with sacro-iliac disorder have a high sedimentation rate, while in others it is normal, the radiological appearances being identical in both?

I think it would be reasonable to insist that a diagnosis of spondylitis should not be made—or at least used in statistical conclusions—on the ground of sacro-iliac changes, unless the sedimentation rate is materially raised or there are spinal changes of characteristic type in addition.

It is my firm opinion that the view held by many that ankylosing spondylitis is simply rheumatoid arthritis affecting the spine has done much to retard progress in its study and to mask some of its most important characters. That there are many analogies must be recognized, but the differences are important.

In the report of the committee of the Royal College of Physicians on nomenclature in arthritis there is a section in which two forms of rheumatoid arthritis are described under the names, "atrophic arthritis", and "chronic infective polyarthritis", though it is admitted that it is often difficult to separate the two. An important sex difference is noted, the former being more common in women in a ratio of nine to one and the latter being only three times more common in women; the former occurring in the child-bearing age and the latter at all ages. It is not definitely claimed that the two forms are essentially different, but the point is submitted for discussion. I think that many who have had a wide experience of rheumatoid arthritis will admit that there are grounds for the division. My reason for mentioning this is that I think there may likewise be two different forms of ankylosing spondylitis, the one described by Gilbert Scott as adolescent spondylitis, and another which begins at a later age; the former being much more acute and progressing rapidly in a centrifugal way, missing no joint and often resulting within a year or two in complete rigidity of the whole spine, the sacro-iliac and hip joints, and often the knees; and in the other direction, the costo-vertebral, sterno-clavicular, and the mandibular joints. It is in this form that the predominance of the male sex is most pronounced. The other, starting in the later twenties or even as late as forty, is slower in progress, the sacro-iliac joints are not affected to the same degree in the early stage, and the progress—while centrifugal—has not the same uniformity, the maximum changes in the spinal column being often in the dorso-lumbar or even in the cervical region and the predominance of the male sex being less pronounced. If such a difference is recognized it would explain many of the divergences in statistics dealing with the sex incidence as well as other features. I think that much confusion has arisen from statistical tables drawn up without sufficient emphasis on exactitude in diagnosis and consequently with typical cases mixed with borderland conditions. It is well known that the disease has a tendency to become quiescent or even to undergo complete cure at any stage, and this may explain the difference between the two types, but I do not find it adequate and I think the matter deserves further study.

The term "ankylosing spondylitis", while descriptive of the most obvious pathological and radiological characters, has the drawback of suggesting that ankylosis affecting the vertebral column is peculiar to the disease; but as Lawford Knaggs and later Oppenheimer have stressed, ankylosis is met with in other diseases, especially tuberculosis. It is to be noted, however, that ankylosis in rheumatoid arthritis is different in character, in that it is the sequel of damage to and breaking down of the articular surfaces; in spinal osteo-arthritis it is due to fusion of osteophytes by synostosis; but in ankylosing spondylitis ankylosis is a relatively early development and is due to deposition of calcium in the ligaments and fibrous tissues adjacent to the bones without destructive changes in the bones having taken place to any extent, and often not at all; even when the hips become completely ankylosed the unbroken outline of the bony surfaces can often be seen in radiographs. Osteoporosis is often extreme, and it appears that the calcium removed from the bones is redeposited in the fibrous tissues in the vicinity, due, it has been suggested, to variation in the *p*H of the body fluids. The calcification of fringes of periosteal tissue along the bones of the pelvis is often a striking feature, as is the ankylosis of the symphysis pubis which sometimes occurs. These features are never seen in rheumatoid arthritis so far as I am aware. Hilton Fagge, in the report he made on a case in 1877, described "a white mortar-like substance filling the cancellous spaces of the heads of

the ribs, the femur, and elsewhere including the surface of the arches of the vertebrae ". Ehrhardt's case presented some similar features.

Tuberculous disease of the spine often displays a similar process of ossification, the ligaments undergoing calcification in the same way, and in this connexion it is noteworthy that positive tubercle skin tests are much more common in spondylitis than in rheumatoid arthritis.

The difference in the sex incidence has already been referred to and is so well known that I need not dwell on it further. It seems evident that endocrine influences are responsible, and the internal secretion of the prostate has been suggested as a factor, but the evidence is thus far inadequate.

The focal cellular accumulations in nerve sheaths and muscles, which were first described by Freund and his colleagues and were confirmed in this country by Kersley, Gibson, and Desmarais, are a very important contribution to our knowledge of rheumatoid arthritis, indicating that it is a general disease not confined to the joints. They have not been found in spondylitis up to the present.

Recently a further discovery in the biochemical field has been made which may prove of importance. Roland Davison has studied 17-ketosteroid excretion in arthritis and has found no change from normal levels, but in spondylitis there is a great increase in its excretion which undergoes marked reduction under *x*-ray treatment and may be brought down to normal levels. This touches the important subject of *x*-ray therapy, which will be dealt with by experts during the discussion. Its value in spondylitis is now generally recognized and is in contrast with its effect in rheumatoid arthritis. A further contrast exists in the effect of gold in the two diseases.

Matheson has recently reported a case at a meeting of the Medical Society of London of bilateral calcification in the kidneys in a woman suffering from ankylosing spondylitis. This is of considerable interest in view of the part played by the phosphatases in inducing calcification, and in a previous paper I referred to this possibility in the kidneys. (Films and photographs of Mr. Matheson's case were here shown.)

ANKYLOSING SPONDYLITIS

NORMAN CAPENER

There is little new or which offers much encouragement in the orthopaedic treatment of spondylitis. A way must be found for treating this disease adequately before the need for surgery arises, for generally when this need is considered to be present the biological conditions of the whole locomotor apparatus are so bad as to vitiate the results at which one aims. The treatment must be based upon a sound knowledge of pathology. In this disease we do not seem to be much nearer having this. Why does the disease so frequently start in the sacro-iliac joints and why does it spread centrifugally from there (with a preference for an ascending course) to the intervertebral, posterior apophyseal, costo-vertebral, and root joints of the limbs? What is the evidence that these are infective lesions? If the disease were due to a blood-borne infection, one would scarcely expect such a peculiar regional origin and dissemination. Is the bone and joint disease merely a local manifestation of a general constitutional disorder such as rheumatoid arthritis or hyperparathyroidism? Thinking upon these questions I am lead to believe that the disease starts as a local one in the pelvic joints and that it later becomes a constitutional degenerative disease effected by the devitalizing influences of fixation and deformation of the costo-vertebral skeleton.

The spread of spondylitic lesions calls to mind the dissemination of prostatic cancer, through the lymphatics to the neighbouring bones of the pelvis and spine. Buckley has recently discussed this and he probably will agree that further study along these lines might be of importance. It is worth mentioning perhaps the well-known relationship of prostatic function with phosphatase and bone formation.

One recent writer states that cases of ankylosing spondylitis require treatment along psychosomatic lines. While it is true that several of my patients became considerably upset by being treated as malingerers in the Army, I have been impressed by the small part that psychological factors play when once the malady has been correctly diagnosed and is under efficient treatment. They are amongst the most co-operative and optimistic of all patients; often putting to shame men with much less cause for depression.

Non-Operative Treatment.—It is generally agreed that during the active phase rest is important. Nevertheless I do not subscribe to the view that this means complete rest. It is, I think, important to stress this, for all too often " complete rest " is interpreted by the unintelligent as " laisser faire ". Therefore this phrase should not be in the vocabulary of medical literature. Physiological rest as we understand it today means the process of giving control of part or the whole of the body in the posture most favourable for the biological processes of growth and repair; it means rest to the maximum extent required for the particular disease being treated, and, consistent with this, the minimum for the restoration of function (locally and constitutionally). It is rarely absolute or uninterrupted

rest. Its purposes are to promote healing by reducing the physiological demands, by avoiding the aggravation of pathological processes, and by making available the whole metabolic resources of the patient. It must prevent the deforming influences of extrinsic forces such as gravity, and of intrinsic forces such as unbalanced muscular activity.

A statement of this sort summarizes the medical strategy of the campaign against any arthritic problem. The tactics of the various medical units concerned with treatment must be co-ordinated along these lines, however much the armamentarium of each may differ.

In preventive orthopaedics our chief aim is to offer guidance in the mechanics of rest and of its graduation. Elsewhere [1] I have recently discussed the general principles in relation to the splintage of arthritic joints. Treatment should be guided by the fact that there is present marked disorganization of the lower spinal reflexes and that there is a striking resemblance between the overpowering inhibition of voluntary motor power and the more complete loss found in a peripheral nerve injury or in anterior poliomyelitis. We must give assistance to the deficient motor units. The gross inhibition and atrophy of the extensor mechanism in spondylitis is one of the most glaring features, the answer to which cannot be found in the complete disclaimer of all forms of external support.

In the use of rest, support, and exercise, uncommon sense and a balanced judgement are needed.

However useful the plaster jacket may be in the treatment of osteo-arthritis and intervertebral disc lesions, there is little place for it in care of ankylosing spondylitis. Even the plaster-of-Paris shell or bed requires very special precautions, for though it need not cause visceral embarrassment, nevertheless for spondylitis more than usual care must be taken to maintain warmth.

In both early cases and those requiring correction of deformity I prefer to use the Bradford frame or one of its modifications. Immobilization on such a frame for part of the day is alternated with activity as symptoms subside. Many apparently rigid spines show a marked improvement of the deformity by head traction upon an inclined Bradford frame. The maintenance of correction is the great difficulty. Spinal supports (of which I use chiefly the Taylor brace) are merely temporary aids. The apparatus should be regarded not as a passive splint for the bony deformity but rather as assistance to weak spinal muscles while they are being re-educated. The sheet anchor of muscular treatment is the improvement of respiratory movement and visceral tone.

[1] *Brit. med. J.*, 1946, 2, 761.

Surgical Treatment.—The correction of deformity can often be achieved readily by the straightforward operation of osteotomy. For the hip, where this is sometimes done, the procedure is relatively simple and healing is rapid. Caution is needed in selecting cases for osteotomy at the hip, for it is not always helpful to correct a flexion deformity when by so doing one only gets a man on to his feet at the expense of his ability to sit down. Actually such osteotomies are very rarely required.

For the spine some form of osteotomy may more often be necessary but of the procedure I have no personal experience. Dr. Smith-Petersen [2] has recently described his method which I saw him carry out in Boston last year. In Smith-Petersen's work it has been shown to be sufficient to carry out multiple osteotomy with resection through the posterior apophyseal joints. La Chapelle of Amsterdam [3] has described a case in which a two-stage osteotomy was carried out. The first combines excision of the laminae of the second lumbar vertebra with removal of the articular facets of this with the third lumbar vertebra, followed at a later date by osteotomy of the second lumbar intervertebral disc by the transabdominal approach with the insertion of bone grafts in the gap produced.

Apart from the correction of deformity the ideal of the surgical approach should be to restore free, painless movement in ankylosed joints. In the more obvious cases in which this is demanded, the biological conditions present render reconstructive surgery almost useless in the present state of our knowledge. Let us remember the profound loss of muscle, the inactivity of the lower motor reflex system, and the atrophy of bone; then the reasons for failure will be obvious.

Various types of reconstructive procedure for the hip are available (e.g., Whitman's reconstruction, Colonna's operation, Girdlestone's hip excision, Jones's subtrochanteric pseudo-arthrosis). The trouble with all these procedures (apart from the neuromuscular problems) is the exposure of a large area of raw atrophic bone, and that if fascial flaps are interposed these are almost certain to become ossified and movement lost. By the older method of arthroplasty by fascial flap I have obtained a worth-while result in only one case.

Since the end of the war I have been doing more arthroplasties using Smith-Petersen's metallic cup interposition. So far I cannot say whether the results are going to be much better. Smith-Petersen himself regards ankylosing spondylitis as the least favourable group for the procedure.

As to the future of surgical treatment in these

[2] *J. Bone Jt. Surg.*, 1945, 27, 1.
[3] *Ibid.*, 1946, 28, 851.

advanced cases of ankylosing spondylitis—it seems to me that better results would be achieved if only mobility of the costo-vertebral joints could be produced. I hope that soon the thoracic surgeons will describe some form of costo-vertebral arthroplasty, which technically should not be at all difficult. But perhaps by then the physicians will have discovered a cure which will render this unnecessary.

RADIOTHERAPY OF ANKYLOSING SPONDYLITIS

D. I. G. WILLIAMS

I propose to describe the radiotherapy of ankylosing spondylitis under several headings: the technique; the indications; contraindications; the hazards and dangers; the rationale, including (a) pathological, and (b) clinical; and lastly the results of such treatment.

Technique.—*X*-radiation therapy for this condition was first used and popularized by the late Dr. Gilbert Scott. He published his papers in 1937. Scott taught that irradiation of the whole trunk with *x* rays of low intensity and in small doses produces constitutional effects. This results in raising the general resistance to disease, being comparable to the effect of ultra-violet light only a hundredfold more effective. This, he implied, meant treating the disease through the patient, thus enabling the patient to gain an ascendancy over whatever pathological condition he might be suffering from. He taught that nature's defence to disease, whether it is typhoid or pneumonia, is simple and the same, and he aimed at raising this defensive mechanism to its maximum power. His evidence was based on the improved blood picture, the lowered sedimentation rate, and the effect on general metabolism as shown by gain in weight and increased feeling of well being. He laid down strict details of the treatment, which was carried out in a variety of diseases ranging from phobias to asthma and rheumatic diseases.

Based on his experience in the treatment of about 200 patients with ankylosing spondylitis, Scott believed that if such treatment were begun before the spine became involved, there was no reason why this tragic disease could not be wiped out.

His method has been tried extensively in many clinics, and there is no doubt that the results are not as good, that is, relief of pain is not so marked, as when intensive localized deep *x*-ray therapy is used. Many cases treated by baths return for localized therapy later—to be more permanently relieved of their symptoms. We use rays generated at 200 to 250 Kv. and filtered through 1 mm. cu.—that is, a hard, penetrating beam. The sacro-iliac joints are covered by one field, and the whole length of the spine is divided into segments 20 by 10 cm. Two fields are treated daily, 300 r units being given to the skin of each field. This is continued in rotation until the skin over the whole spine and sacro-iliac joints receive a dose of 2,000 to 2,400 r, the actual involved joints in the spine receiving about two-thirds of this dose. Treatment thus involves daily attendance for a period of three weeks.

If other joints are involved, for example the hips or shoulders, these are treated to the same dosage after the spine is completed. Sometimes patients complain of pain in odd sites, such as ischial tuberosity, the crest of the ilium, the sterno-clavicular and costo-sternal joints, etc. These respond to *x*-ray therapy in the same way, localized fields over the affected part being used.

Rationale of X-ray Treatment.—Why do we get results? I do not know. At one time I thought we were pouring an unknown ray—the *x* ray—into a disease of which we knew less. Steinberg in 1942 described the pathological process as a proliferation of synovial membrane cells producing a layer of vascular granulation tissue over the articular cartilage, with simultaneously a similar change in the connective-tissue elements of the bone marrow below the articular cartilage. This latter reaction extends through the zone of provisional calcification so that the articular cartilage is destroyed by the two granulations. These two layers of granulation tissue have marked potentialities for forming fibrous tissue and bone. If this is so then it is an inflammatory reaction which we know is radiosensitive and in which resolution can be induced by means of *x* rays. Why one gets relief of pain in the old-standing case with bony ankylosis, I do not know.

The Dangers of Treatment.—This form of treatment is not without its dangers (1) to the skin, (2) to the blood, and (3) to the generative organs.

To the Skin.—Owing to back scattering from the metallic elements in bone, skin over bony prominences shows a greater reaction than skin with a soft-tissue bed. Bearing in mind that orthopaedic treatment may be necessary, involving hard beds, etc., no case should be taken beyond a dry, scaly, desquamative skin reaction. During treatment the skin should be kept dry with spirit and powder, and washing with soap should be avoided.

To the Blood.—It will be appreciated that when the spine of young people is irradiated a large volume of bone marrow is exposed. In the chest, the heart with its large volume of circulating blood is exposed to radiation. Both these factors contribute to the characteristic radiation effect on blood, a leucopenia chiefly affecting polymorphs, with later lymphocytes and later still a fall in the red cell

count. These reactions are guarded against by weekly complete blood counts, more frequent if the count is low, and the administration of tonics, vitamins, and iron, whilst of course good food, fresh air, sunlight, etc., are very important. These measures help to counteract the so-called general or constitutional reaction.

Constitutional Reaction.—This is manifest by lassitude, nausea, vomiting, and prostration. All patients complain of tiredness and lassitude to some degree. The more severe symptoms, vomiting, etc., are not very common, but when sickness does occur it may be relieved by benadryl, 50 mg. by mouth or by injection (benadryl is an antihistamine substance) and an increase in the amount of salt in the diet.

Effects on the Organs of Generation.—If the testicles come within the beam of the *x* rays they should be protected by lead shields—a comparatively simple procedure. In the female, the ovaries cannot be protected. If they lie within the irradiated field and the sacro-iliac joint cannot be adequately irradiated without exposing the ovaries, the dose which reaches them will almost certainly induce an artificial menopause, either temporary or permanent, or at least menstrual irregularities. The symptoms of an artificial menopause under the age of 40 tend to be severe, and the danger should always be explained to the patient. The symptoms can be minimized by the administration of oestrogens, but there is a further factor which makes one hesitate to advise irradiation in young women. Even small doses of irradiation may result in microscopic changes in the generative cells—chromosome abnormalities, and there is experimental proof in animal experiments that these changes are irreversible and transmitted. The chances of producing monsters, idiots, etc., in the immediate succeeding generation are probably small, but later generations may show developmental abnormalities. We do not know, and these facts cannot be explained to the patient; but I would advise against irradiation in any young woman who desires children. If they do not wish for children then the reactions must be explained and the choice left to them.

The Effects of Treatment on the Disease.—One can classify the disease into three broad groups: (a) early: with changes confined to the sacro-iliac joints; (b) moderately advanced, partially or completely obliterated sacro-iliac joints, and some involvement of the spine, chiefly the posterior articulations; (c) the advanced group, with ossification of the common ligaments.

The effects of *x*-ray therapy are as follows: (1) pain is decreased or abolished; (2) because of this, paravertebral muscle spasm is relaxed; (3) stiffness is less, and there is increased spinal motion and chest expansion; (4) probably the most important result of relief of pain is that it allows patients to carry out orthopaedic treatment more easily and more freely.

With relief of pain and increased mobility, the whole mental outlook changes. Many have suffered for months. The failure of other methods of treatment leads them to believe that cure is not possible. As a result of *x*-ray treatment their general health improves, they gain in weight, and toxaemia, of which one evidence is a raised sedimentation rate, is reduced. This is taken as evidence that the activity of the disease decreases, although marked discrepancies do occur between the clinical condition and the sedimentation rate. The patient returns to his work, and this of course contributes to his mental happiness.

In early disease the patient may regain full movement. It is my practice, even when the clinical and radiological evidence points to involvement of the sacro-iliac joints, to irradiate up to the cervical spine. In the moderately advanced group pain is abolished in almost every case, but the range of spinal movement may remain restricted. Even in advanced cases, some relief of pain is obtained.

I know of cases treated seven or eight years ago—one seven-year advanced case with whole spine and hip involvement who remains free from symptoms to date. Can *x*-ray therapy arrest the disease? I believe it does, or at least retards the progress. I always tell my patients that pain will be removed, mobility increased, and the disease arrested.

If recurrence of symptoms occurs after a full course of *x*-ray therapy, then the treatment can be repeated at least once, but I would advise that the patient be seen by the therapist who gave the first course. Re-treatment should not be considered within a period of six months.

I would suggest, therefore, the following plan of treatment for ankylosing spondylitis. The first step is *x*-ray therapy. At the conclusion of treatment the patient should be referred back to the orthopaedic department for corrective treatment and supervision, for the prognosis—apart from the stage at which the disease is diagnosed and the adequacy of radiotherapy—depends most of all upon the subsequent orthopaedic care of the patient. He should remain under medical care for a long time, and further therapy may be called for if he develops pain in other sites.

Discussion on Spondylitis

Dr. G. D. Kersley said that Dr. Williams had given a fair account of the *x*-ray treatment and the dangers of toxic symptoms. But the thing he himself was convinced about was the danger of the big dose. He believed that equally good results could be obtained from very much smaller doses. The difficulty was to get a truly comparable series of cases with these different doses. The total dosage Dr. Williams had been using, he believed, was 2,400 r; others had been using a dosage of 800 to 1,000 r, and as far as he could gather the results were equally good. But no properly worked out series

with controls had been established and that was a thing which ought to be done.

DR. F. BACH recalled Mr. Capener's remark about the keenness and enthusiasm of his patients for treatment. These people were of a particular type. In the early stages they seemed to have the physique which the modern American methods of Draper and Sheldon had shown to be quite definitely characteristic, both constitutionally and psychologically. It was the person of a certain type who was going to get this disease, and therefore their studies should be directed more and more, perhaps, towards constitution and they should receive the help which Americans were receiving in other fields concerned with rheumatic disease, such as studies of heredity and so on. Dr. Mabel Wilson seemed to show that in rheumatic fever also there was a hereditary factor. It was found again and again that there were many cases of spondylitis in particular families. Although full consideration should be given to the points which Dr. Buckley had brought forward, he still thought that in their studies the natural history of the disease should be stressed, and the physician should be aware of the family history and the psychological and constitutional background.

Dr. Bach thought that in early cases there was a great deal of spasm, especially of the erector spinae muscle. Recently at St. Thomas's he had had one or two cases in which he thought the spasm very marked, and he had asked Dr. Bauwens to investigate them for him; yet to his astonishment they showed no evidence, by modern methods, of spasm.

DR. E. G. L. BYWATERS thought that caution should be exercised before coming to conclusions about the typing of ordinary patients. Particularly in pathological classification some hesitation was necessary. It was very important that, with the surgical approach, adequate biopsy material should be studied. It was very difficult to distinguish between the factors of heredity and environment. He mentioned a case in which two girls—sisters—were supposed to have typical spondylitis. One girl was ten years older than the other, and in both the onset of the spondylitis had occurred at the age of 18.

MR. W. D. COLTART said that it had always seemed to him that they should leave the question of aetiology to the physician and the relief of pain largely to the radiotherapist. They could, he thought, probably prevent deformity from arising in some cases. The use of the plaster bed and of proper exercises to regain tone and power of the muscles would sometimes prevent the onset of deformity; at least some cases did not develop that deformity while that treatment was proceeding. Once deformity had arisen he very much doubted whether they could succeed in correcting it. Sometimes, after several months in a plaster bed, there was some improvement, but the case soon relapsed. With regard to restoration of mobility to the spine one could, perhaps, preserve a little movement, but to increase the range of movement in ankylosing spondylitis was almost impossible by ordinary methods. It was rather a depressing view of what they could do as orthopaedic surgeons.

A young woman, the wife of a colleague, had developed ankylosing spondylitis three or four years ago. The only thing known to be likely to prevent the progress of the disease was *x*-ray treatment. She had asked him what was the percentage of permanent sterility as a result of *x* rays.

With regard to out patients and in patients, he thought that with *x*-ray therapy it was very much better to have out patients. There was a slight difference in response to treatment as between out and in patients.

MR. N. L. CAPENER said he did not feel quite so depressed about orthopaedic treatment in the early stages as Mr. Coltart had confessed to being. Certain differences were to be noted between the civilian patient and the Ministry of Pensions patient. With the former the results were not so good, but there were not the beds available for dealing with civilian cases in the same way as with pensions cases; if there were, better results might be obtained.

DR. WILLIAMS said that the subject of *x*-ray sterilization was very difficult. There were no figures to be quoted, but he could mention the case of a young girl of 21 or 22, with a normal menstrual history, who was treated on one side of the iliac fossa for a keloid scar, receiving 700 r to the skin, and was sterilized. He did not think there was any way out of it. The patient would certainly be sterilized and an artificial menopause induced. He had tried to compromise in a recent case by using very small fields—strip fields very accurately localized to the sacro-iliac joint. She was a girl of 17 who was in considerable pain. It was necessary to treat both the iliac sacral joints and the lumbo-sacral and neighbouring joints, and along the spine. Personally he would not like to treat with *x*-ray therapy a patient desirous of having children.

DR. BUCKLEY, in replying on the discussion, said that Dr. Williams's observations on sterility had been of extreme interest. In the *Journal of Radiology* he noticed a statement by a radiologist who started his work at the Holzknecht clinic in Vienna saying that the sacro-iliac joint should never be treated by means of *x* rays. He declared that such a procedure did no service whatever, and that equally good results would be obtained by concentrating treatment above the lumbo-sacral junction. That might solve some of the problems which had been raised in that discussion. If good results could be obtained from the application of *x* rays above the level of the lumbo-sacral joint then the danger of sterility might be escaped.

With regard to the question of family tendencies, this was reviewed rather thoroughly in the Proceedings of the American Rheumatism Association. There were two opposite views. One group of investigators found family tendencies very pronounced, and another found them very rare.

One point which must always be borne in mind in all these statistics, not only concerning radiotherapy but also other treatments, was the marked tendency of ankylosing spondylitis towards quiescence, and also the tendency it displayed for complete and early cure without any special treatment beyond the general building up of the patient.

THE MORBID ANATOMY AND HISTOLOGY OF RHEUMATIC LESIONS

G. D. KERSLEY and M. H. L. DESMARAIS

Dr. G. D. Kersley said that in rheumatoid arthritis lesions had been discovered in a very wide distribution throughout all the connective tissues of the body—even at sites where no clinical evidence of disease existed. They were first described in America [1], [2], [3], and this work has been largely controlled and amplified by studies carried out at the Royal National Hospital for Rheumatic Diseases, Bath.[4] The lesions consisted of: (1) peri- or para-vascular accumulations of lymphocytes with, in some cases, plasma cells and occasionally eosinophils; (2) degenerative and proliferative changes in all coats of the small blood vessels; and (3) degenerative changes in the muscle fibres, probably secondary to the aforementioned changes.

This histological picture was found in any or all the muscles of the body at any stage of the disease, and the foci of round cells and vessel changes also in the synovial membrane, the fibrous stroma of fatty tissue, and around the peripheral nerves. In the course of about 100 biopsies this histological picture had not so far been seen in any typical rheumatic condition other than rheumatoid, non-specific, infective, or atrophic arthritis. It had not been seen in ankylosing spondylitis. (Sections of muscle, joint tissue, pericardium, nerves, and subcutaneous fatty tissue were shown.)

The Histology of Nodules.—Nodule formation in rheumatoid arthritis was very similar to that seen in certain cases of rheumatic fever, but the lesions could be distinguished with considerable certainty under the microscope. Distinguishing features were the size of the central necrotic zone, which was surrounded by a palisade layer of radially arranged mesenchymal cells, and outside this was a fibrous stroma in which lymphocytic foci of the rheumatoid type might often be seen.

Five common types of nodule, clinically and histologically characteristic, had been described; those occurring in rheumatoid arthritis, rheumatic fever, gout, fibrositis, and fibrous nodules which appeared on the hands attached to the extensor tendon sheaths.[5] Cholesterol was found in many of those of both gouty and rheumatoid origin.

" Fibrositis " might have a dual pathology, fatty herniae, and localized spasm of muscle fibres.[6], [7] (Slides showing the histology of each type were shown.)

Dr. M. H. L. Desmarais said that a further series of 95 cases had subsequently been investigated at the Royal National Hospital for Rheumatic Diseases, Bath. Of 30 cases of idiopathic rheumatoid arthritis, 25 biopsies showed the typical round-cell foci and 5 were negative. One case was negative at biopsy but proved to be positive when a large piece of muscle was excised at operation.

The remaining 65 cases covered a wide range of other types of rheumatic and non-rheumatic conditions and were all negative except for two positives in 2 cases of rheumatoid arthritis simulating gout and one positive in 3 cases of rheumatoid arthritis associated with psoriasis.

Twelve cases of spondylitis ankylopoietica, 4 of gonococcal arthritis, 2 of Still's disease, and 4 of osteo-arthritis were *all* negative.

This material will be the object of a paper in which the findings will be discussed in fuller detail.

RELATIONSHIP BETWEEN PULMONARY OSTEO-ARTHROPATHY AND RHEUMATOID ARTHRITIS

E. G. L. BYWATERS

Dr. Bywaters spoke of radiological similarities between rheumatoid arthritis and pulmonary osteo-arthropathy which might throw light on the mechanism of the latter.

He first described a case of pulmonary osteo-arthropathy due to metastatic hypernephroma, which had originally been diagnosed as rheumatoid arthritis because of acute onset of pain, swelling, and effusions in the knees, ankles, and wrists. This mode of onset, he said, was well recognized; the clinical signs preceded any radiological abnormalities in the bones. Radiographs and sections showed a periosteal shell of new bone and a slightly oedematous periosteal membrane: this change affected all bones of the hand and forearm, including the non-articular surfaces of carpal bones.

A similar appearance was noted in the neighbourhood of swollen and inflamed joints in 6 cases of rheumatoid arthritis: it was very marked in childhood, producing " rheumatoid dactylitis ", but was seen also in a patient whose illness started at the age of 69 years. Serial radiographs showed that it developed rapidly during the acute phase: it was often accompanied by pitting oedema in the neighbouring tissues. Some rheumatoid arthritis cases showed an inflammatory oedema for some months before the joints became obviously involved. Such

[1] Allison, N., and Ghormley, R. K. (1931). " Diagnosis in Joint Diseases." New York.
[2] Freund, H. A., Steiner, G., Leichtentritt, B., and Price, A. E. (1942). *Amer. J. Path.*, 18, 865.
[3] Steiner, G., Freund, H. A., Leichtentritt, B., and Maun, M. E. (1946). *Ibid.*, 22, 103
[4] Gibson, H. J., Kersley, G. D., and Desmarais, M. H. L. (1946). *Annals of the Rheumatic Diseases*, 5, 31.
[5] Kersley, G. D., Gibson, H. J., and Desmarais, M. H. L. (1946), *Ibid.*, 5, 141.
[6] Copeman, W. S. C., and Ackerman, W. L. (1944). *Quart. J. Med.*, 13, 37.
[7] Elliott, F. A. (1944). *Lancet*, 1 ,47.

periosteal changes were not seen in cardiac or renal oedema where tissue fluid protein was below 1 g. per cent.: in rheumatoid arthritis the tissue fluid clots and contains over 2 g. per cent. protein. It seems possible that the presence of such an inflammatory oedema may directly produce the periosteal change. The latter was not specific for rheumatoid arthritis, as it was seen in other chronic bacterial arthritides.

Such an explanation would not be impossible for pulmonary osteo-arthropathy, where there was a fairly high content of protein in the joint fluids, compared with much lower levels in the hydrarthrosis of cardiac oedema. It was hoped to collect further data on this point, since, apart from Mendlowitz's suggestion of an alteration in haemodynamics, little was yet known of the pathogenesis of the changes in clubbing and pulmonary osteo-arthropathy.

PENICILLIN FOR THE RHEUMATOID TYPE OF ARTHRITIS

FRANCIS BACH

The general clinical impression is that the results of penicillin in the treatment of many rheumatic disorders have been disappointing. Few reports on its use have been made in this country, but in the United States and in France small series of cases have been recorded.

On July 5, 1946, at a joint meeting of the Section of Internal Medicine and that of Experimental Medicine and Therapeutics held in San Francisco, Philip Hench said: "There are actually about two hundred forms of rheumatism, including about one hundred different types of arthritis. But approximately 85 per cent. of rheumatic patients suffer from one of seven common conditions: rheumatoid arthritis, osteo-arthritis, the polyarthritis of rheumatic fever, periarticular or intramuscular fibrositis, psychogenic rheumatism, gout, or gonorrheal arthritis."

He said that, in cases with a supposed relationship between haemolytic streptococci and rheumatoid arthritis, it was hoped that penicillin might be of value; however, large doses of penicillin have been given intramuscularly daily for from three to six weeks, or even orally daily for from one to six months, but no significant benefits were noted.

He had been able to find, in the literature on penicillin between 1943 and 1946, only 82 cases of gonorrhoeal arthritis treated with penicillin. Of these, only 20 were of proved gonorrhoeal arthritis. The remaining 62 he classified as presumptive gonorrhoeal arthritis. In 11 of the 18 proved cases, cure was obtained. Of the 59 cases with presumptive acute gonorrhoeal arthritis, 34 were cured and 25 not. He concluded that gonorrhoeal arthritis, despite certain reports to the contrary, is generally cured promptly when enough penicillin is given. Most of the failures apparently occurred when dosage had been inadequate; some were due, he thought, to errors in diagnosis which had led to the treatment of patients with genital gonorrhoea whose associated arthritis was non-gonorrhoeal.

He emphasized that rheumatoid arthritis can be precipitated, reactivated, or aggravated by acute gonorrhoea, which is one more infection which, like influenza or tonsillitis, can act as a trigger mechanism. He said that at one of the Army's rheumatism centres cases of post-gonorrhoeal rheumatoid arthritis were more common than cases of gonorrhoeal arthritis. Penicillin cured the genital gonorrhoea, but not the associated or constitutional rheumatoid arthritis.

Rantz [1] and his colleagues reported on the administration of penicillin in the treatment of 6 patients with rheumatic fever, in all of whom group A haemolytic streptococci were eliminated from the nasopharynx. Penicillin had not favourably affected the course of rheumatic fever.

In France, Coste and his fellow workers [2] concluded that the best results were obtained in gonococcal rheumatism, in particular in its early, active, and non-articular forms. In infectious rheumatism, out of 14 cases they had 7 good results. These cases they classified as following tonsillitis, influenza, scarlet fever, and infection of the teeth. The treatment was unsuccessful in 19 of 28 cases of rheumatoid arthritis, and in 7 cases there was marked clinical improvement. In 6 of 22 cases of spondylitis "rhizomélique", the clinical results were good.

Weinstein[3] described five cases of complicating infections occurring during treatment with antibiotic agents, two following penicillin therapy and the others following streptomycin. He held that in all these the second infection was produced by organisms normally present in the nasopharynx and was not the result of the introduction of accidental bacteria. The spontaneous occurrence of new infections due to non-susceptible organisms during the course of penicillin or streptomycin therapy raised the question of the use of either of these drugs in instances where the exact bacteriologic diagnosis is unknown, because patients may be exposed to the added danger of superimposed bacterial disease without benefit to the primary process. He suggested that the treatment of virus infection with either streptomycin or penicillin may be dangerous because these drugs have no effect on the primary disease and may allow organisms that are normally present on various tissues and are not susceptible to their activity to grow profusely and invade. The mechanism is not clear, but it is possible that in some persons a high degree of bacterial antagonism exists in areas like the nasopharynx, and that certain groups of bacteria are kept in check by others.

I have used penicillin in the treatment of acute and chronic rheumatism. In rheumatic fever the results have been difficult to assess. In the few cases of gonorrhoeal arthritis that I have followed up, they have been encouraging. In Reiter's syndrome and abacterial pyuria they have been uncertain. A

[1] *Amer. J. Pediat.*, 1945, **26**, 576.
[2] *Sem. Hôp. Paris*, 1946, **22**, 1897.
[3] *Amer. J. med. Sci.*, 1947, **214**, 56.

patient of mine two years ago had an acute attack of urethritis and arthritis which was treated with penicillin, and which cleared up, leaving only stiffness of the feet and ankles, and this was relieved completely with physical treatment. One month ago he had an acute flare-up, with swelling and pain and much free fluid in his right knee; he had swelling of the right ankle, and conjunctivitis, and purulent urethritis. The venereologists' reported that gonococci could not be isolated from the urethral joint fluid. He has had several million units of penicillin. The urethritis and conjunctivitis have cleared up and the pain and swelling in the right ankle has gone but the right knee is still acutely painful and swollen.

That joint changes may occur in patients with diseases of the lung is an old observation. In the *Lancet* of March 22, 1947,[1] there was an annotation on joint changes in cancer of the lung. It was noted that joint changes are occasionally recognized in cases of pulmonary carcinoma and other lung tumours and may even be the earliest feature which brings the patient to the doctor. In such cases the joints may have been treated as rheumatic without benefit. They are characterized by constant and distressing pain in the joints, a polyarthritis affecting principally the wrists, fingers, and ankles; less often, elbows, knees, and spine. There is considerable swelling of soft tissues, and, when the classic picture is present, clubbing of the fingers—and the characteristic radiographic changes, such as the periostitis at the distal ends of the tibia and femur of pulmonary hypertrophic oesteopathy are seen. The annotator wrote, "There is no satisfactory explanation of the association of joint and lung conditions or whether extensive tissue breakdown or infection is the trigger or linking factor. Endocrine disturbances may play a role, but attention must be given to sepsis from breakdown of the growth."

The arthropathy may be dramatically relieved by removal of the lung.

Within the last 3 years, 4 of such cases have come under my care, all of which had been referred to me as suffering from rheumatoid arthritis—a wrong diagnosis. In two cases, marked improvement, with relief of pain and marked diminution and almost complete disappearance of the joint swelling followed deep *x*-ray treatment to the chest. In one case, when this was combined with penicillin therapy, there was marked clinical improvement.

In "infective" arthritis associated with severe bronchiectasis, penicillin therapy followed by lobectomy has been followed by improvement in general health and almost complete disappearance of the joint swelling and return of the normal range of joint movement.

[1] *Lancet*, 1947, 1, 378.

At present I have under my care a girl, 21 years of age. Four years ago, she had a second attack of pleurisy; this was followed by joint pains and progressive swelling of her knee joints, shoulders, wrists, and ankles. Eighteen months ago, she was referred to me as a case of rheumatoid arthritis (a wrong diagnosis). She was tired and markedly under-weight, with painful and swollen joints. Her hands were not involved, nor the epitrochlear glands enlarged. The sedimentation rate was raised. She had no sputum and there were no signs of pulmonary tuberculosis. Detailed examination showed an extensive bronchiectasis of the left lower lobe and lingula. She was given penicillin. Three months ago a chest surgeon performed a left lower lobectomy and lingulectomy. Today she has no pain and, apart from some stiffness of her shoulders, she has full normal joint movements.

For some years it has been my clinical impression that there is more than a chance relationship between the rheumatoid types of arthritis and disease of the lung. On many occasions I have recognized bronchiectasis in patients with rheumatoid arthritis. Last week Tegner, in his Presidential address on rheumatoid arthritis at the Royal Society of Medicine, said that in the last few years he had noticed among his new rheumatoid patients several men who developed the disease when they were past middle age. This has also been my experience, and I found that many of these patients also presented the signs of bronchiectasis. Recently I looked up the records of 12 of my hospital in-patients who presented the picture of rheumatoid arthritis and bronchiectasis. Seven were treated with penicillin, and this small series can be divided into two groups, the one consisting of four men, aged 56, 57, 61, and 62 years; the other of three women aged 16, 30, and 45 years. All the patients in group I received 2,000,000 units of penicillin intramuscularly in 10 days, and inhaled 200,000 units in 8 c.cm. saline during this time.

Case Histories

I (*a*).—A clerk, aged 56, had a typical rheumatoid type of arthritis, with joint manifestations of 4 years' duration, no cough, and no sputum. On one occasion a throat swab yielded haemolytic streptococci. Radiographs showed joints typical of rheumatoid arthritis, and cylindrical bronchiectasis of the right lower lobe. After penicillin treatment the blood sedimentation rate fell from 82 to 38 in the first hour, and the general clinical improvement was good.

I (*b*).—A carpenter, aged 57, had a typical rheumatoid type of arthritis, with joint manifestations of 6 years' and bronchitis of 4 years' duration. He had a slight cough, and the sputum yielded micrococcus catarrhalis and diphtheriae pneumococci. Radiographs of the joints showed a typical rheumatoid type of arthritis, and of the chest a healed bilateral apical tuberculous infiltration. A bronchogram showed cylindrical dilatation of the posterior bronchi of the left lower lobe. After

penicillin treatment the sedimentation rate fell from 50 to 30, with general clinical improvement.

I (*c*).—A clerk, aged 61, had had joint manifestations for 6 years, no cough, and no sputum. No organisms were detected in the throat swab. A radiograph of the joints showed a typical rheumatoid type of arthritis. The chest was of a chronic catarrhal type, and a bronchogram showed cylindrical bronchiectasis in the left lower lobe and slight circular bronchiectasis in the right. After penicillin treatment the sedimentation rate fell from 70 to 18 in the first hour, with definite clinical improvement.

I (*d*).—A railway checker, aged 62, had had joint manifestations for 3 years, and 10 years previously had had a perforated gastric ulcer. There was no cough or sputum, but the throat swab yielded haemolytic streptococci on three occasions. Radiographs showed a typical rheumatoid type of arthritis in the joints, and bronchiectasis in the left lower lobe. The blood sedimentation rate rose during treatment from 60 to 80.

II (*a*).—A housewife of 30 had had joint manifestations for 2 months, with productive cough and loss of weight. There were no tubercle bacilli in the sputum, but micrococcus catarrhalis and haemolytic streptococcus. Radiographs of the joints showed an early rheumatoid type of arthritis, and a bronchogram a moderate degree of cylindrical bronchiectasis in the left lower lobe. When penicillin was given the sedimentation rate rose from 25 to 30 in the first hour. There was clinical improvement and the patient gained weight.

II (*b*).—A housewife of 45 had had joint manifestations for 20 years, and productive cough with sputum for three. The sputum yielded varied growths, but no haemolytic streptococci or tubercle bacilli. Radiographs showed advanced rheumatoid-type arthritis in the joints, and bronchiectasis in both lower lobes. She was treated with penicillin and postural drainage. The sedimentation rate remained stationary, 50 to 46 in the first hour. There was marked clinical improvement.

II (*c*).—A girl of 16, a domestic servant, had had a typical rheumatoid type of arthritis for six weeks, with no cough or sputum but vaginal discharge. No haemolytic streptotocci or tubercle bacilli were found in the throat swab, and no gonococcus in the vaginal discharge. Radiographs of joints showed an early type of arthritis, and of the chest, pneumonitis. Penicillin was given with marked improvement in the general condition, though the sedimentation rate was still raised.

Summary

1. Penicillin is of no proven value in the treatment of the rheumatoid type of arthritis.

2. It has long been thought that infection is an important aetiological factor.

3. The association of rheumatoid arthritis and bronchiectasis is not uncommon, especially in middle-aged and elderly people.

4. In the literature, bronchiectasis has seldom or never been recorded as a focus of infection in rheumatoid arthritis.

5. A brief description of a series of patients with bronchiectasis and rheumatoid arthritis has been presented.

6. Treatment of the bronchiectasis appears to have a beneficial effect on the general health of the patient but, to date, there is no evidence that it had any long-term beneficial effect on the arthritic manifestations of the rheumatoid arthritis.

This is in agreement with the clinical impression long held—that removal of foci of infection by either surgical or chemotherapeutic measures is not followed by dramatic relief of the joint condition. It is in direct contrast to the improvement in the joint conditions which are known to be due to infections of definite infective aetiology such as the gonococcus, the infecting organisms of bronchiectasis, and to those due to specific localized chest tumours which affect the joint metabolism such as carcinoma of the lung. In such cases, penicillin is of definite value in the eradication of the infective or causative agent. But in rheumatoid arthritis associated with presumptive gonorrhoea, as shown by Hench, and in rheumatoid arthritis with bronchiectasis as suggested by me, it will have no such effect.

Penicillin should not be used indiscriminately because it may modify the defence mechanism of the body—evidence for which has been given.

I should like to throw out the suggestion that the patient with rheumatoid arthritis may have an altered *inherited* susceptibility for various infections, as has been shown by May Wilson to be present in patients with rheumatic fever.

MINOR SIGNS OF DISPLACEMENT OF INTERVERTEBRAL DISCS

R. G. ABERCROMBIE

Dr. Abercrombie said that in giving a name to his communication he had advisedly used the term " minor ", since the signs he was about to describe were supplementary to the well-recognized and generally accepted evidence of displacement of the discs. He had frequently found these signs useful in difficult cases.

Plantar Sign.—This sign depended on changes in the tissues of the sole of the foot on the affected side, the changes being of two kinds: an atrophy of the tissues of the sole, giving rise to an appearance of wasting; and an increase in the number and depth of the corrugations of the plantar skin. The sole became wasted, and the shrinkage gave rise to wrinkling of the skin. These changes might either of them be present without the other. Although these signs were often obvious they were frequently overlooked. Indeed, the sole was a kind of blind spot in neurology, in curious contrast with the palm of the hand. The examination of the sole was

physically an awkward one. The patient had to lie flat on his face, with flexed knees, and the two sides compared side by side in a good light, or alternatively he had to kneel on a couch with his back to the observer, the soles being placed side by side. If these small details were not observed, the sign would be missed. The wasting was not due to atrophy of the muscles of the sole but to a loss of substance of the plantar fascia. It usually affected the inner part of the sole, and also sometimes the heel. It had a trophic origin. The plantar fascia was exposed to great and continuous strain; it bore the whole weight of the body in walking and standing. It was in a state of nutritional high tension, and it readily wasted when its innervation was disturbed. This occurred the more rapidly because the fat-globules enmeshed in the plantar fascia were easily absorbed. The wrinkling of the skin was partly due to shrinkage, but also sometimes partly to a semi-involuntary spasmodic contraction of the muscles of the sole. This delicate plantar sign was not invariably present but might occur when there were no objective sensory changes in the skin and when the ankle jerks were quite normal. It did not discriminate between a displaced disc and other forms of irritation of nerves and their roots, but it did indicate that an organic nerve-lesion was present, and that the cause was neurological and not psychological.

The "Forced Expiration" Sign.—In displacement of discs pain was often aggravated by coughing, sneezing, or straining, due doubtless to an increase in the intra-spinal pressure. The sudden violent strain of coughing or sneezing might, however, also aggravate the pain of a fibrositic or myalgic condition of the chest wall or back. Here the "forced expiration" sign might be useful: the patient clasped and closed his nostrils with his fingers and then made an expiratory effort. No sudden violent strain would thus be caused to the muscles or tissues of the chest and back, and if this expiratory effort caused radiating pain, particularly with a radicular distribution, it was evidence in favour of a displaced disc. This sign was perhaps particularly well seen in displacements of the cervical region. In a typical response the patient would be able to release his nose and mark out the site of pain with his finger.

Vertical Lumbar Spine.—This was a radiographic sign, and Dr. Abercrombie said he spoke under correction by experts. When it was present, in the lateral view of the lumbar region there was complete loss of the normal forward curve of the lumbar spine, which stood erect and straight like an architectural column; more rarely the lumbar spine might be actually curved slightly backward. Radiologists sometimes noted this point, but usually not, and he had not seen it mentioned in the literature. Yet the radiographic appearance was far more noticeable than the external, which might be difficult to see in a bulky patient. Doubtless the vertical lumbar spine was due to spasmodic contraction of the spinal muscles. Though it might also occur whenever the spinal muscles were spasmodically contracted, a displaced disc was the most usual cause. A similar sign might occur in the cervical region.

Dr. Abercrombie added that there were several radiographic signs of more importance than the vertical lumbar spine, and he had found radiographic evidence to be of many-sided value—this being in contrast to the experience recorded in Kendall's recent review.

Conclusions.—The question now arose as to the value of these three signs as indications of disc displacement. The evidence was indirect. Laminectomy was only occasionally performed, and contrast myelography and lumbar puncture had been abandoned. Diagnosis at present depended on the history, symptoms and signs, the radiographic appearances, and the clinical course. The signs described had been found to accord with these other elements, and had sometimes seemed to supplement them, and to turn the scale in a case difficult to diagnose.

COLCHICINE POISONING

J. G. MACLEOD and L. PHILLIPS

This communication was published in full in the *Annals of the Rheumatic Diseases* for December, 1947, p. 224.

CLINICAL MEETING

A clinical meeting of the Society was held on Dec. 5, 1947, at the West London Hospital, when Dr. W. S. C. Copeman showed a short film. Full summaries of two of the papers read are given below.

The Treatment of Osteo-arthritis with Procaine Lactic Acid

DAVID P. NICHOLSON

The *Lancet* of Feb. 26, 1938 (p. 487) contained an article by Mr. Grant Waugh of Sunderland, and in this paper he endeavoured to outline a method of treatment that was based on observations of the *p*H of synovial fluid. These observations related to the hydrogen-ion concentration of joint fluid, and within the limits of his experiments he found that following injury or infection the hydrogen-ion concentration, as measured by the *p*H, tended to be acid in the early "reparative" phase, reverting to normal alkalinity in due course.

Unfortunately his experimental observations were limited in number, and the estimation of *p*H crude. In all he appears to have examined fluid from 37 people, 20 with traumatic arthritis, 2 with amputations, 5 with infective arthritis, and 10 with chronic rheumatoid arthritis. Examination of joint fluid from hares and rabbits, and from two human ankle joints obtained from amputated legs at operation, confirmed that the normal *p*H of joints is alkaline.

Mr. Grant Waugh discussed Stirling's observation made in 1932 that the hydrogen-ion content of the primary haematoma around a fracture changes from

alkaline to strongly acid, and he drew the deduction that this allows solution of bone calcium in order that tissue regeneration may occur. On available evidence this deduction may well be a confusion of cause and effect, of ends and means. This local effect may merely be the expression of increased metabolic activity. As regards lactic acid therapy, it is as well to remember this compound's position in the general scheme of the organism. Lactic acid is a normal end-product of muscle metabolism, and is related in the "Krebs" cycle to the respiratory catalysts, succinic and adenylic acids. The latter compound is one of the "metabolites" responsible for local vascular dilatation in ischaemic tissue injury. However interesting are these relationships, it is unlikely that local acid injection would have any general effects. It is a well supported physiological observation that the accumulation of lactic acid in tissues is prevented from causing any alteration in hydrogen-ion concentration by its rapid neutralization with salts, notably bicarbonates. The only exception to this would appear to be in deliberate muscle contraction under anoxaemic conditions.

Mr. Grant Waugh's own observations were unfortunately scanty. Recent work by physiologists suggests that *p*H of body fluids can only be measured accurately by the use of *in vivo* methods. The withdrawal of fluid for *in vitro* estimation may well be associated with a rearrangement of gases between the fluid and the environment: if this rearrangement should affect the partial pressure of such a gas as carbon dioxide the *p*H recorded may belie its *in vivo* value. With the use of glass electrodes and a saturated potassium chloride bridge situated in the buccal cavity, the potential difference being recorded on a Cambridge potentiometer, it has been shown that the *p*H of saliva is relatively more acid than was hitherto believed. Mr. Grant Waugh's observations fall below such exacting standards; *p*H was measured by a B.D.H. capillator after withdrawal of a suitable quantity of fluid; nor apparently were joints affected by osteo-arthritis investigated. From the above inadequate data the author concluded that the development of acidity was a physiological response to trauma "designed" to exact local leucocytosis and repair by mesoblastic proliferation.

Mr. Grant Waugh endeavoured to imitate natural acidification in the process of repair by injecting a stable solution of procaine lactic acid at a *p*H of 5·0 into joints known to be arthritic, but "inactive". In the *British Medical Journal* of June 23, 1945 (p. 873) he was able to state that since his inception of the lactic acid treatment of "arthritic" joints he had in this way dealt satisfactorily with 1,200 cases. By Dec. 7, 1946, the figure has grown to approximately 10,000 cases in his own practice. Originally the injection was followed by immediate manipulation and then rest during the stage of reaction, followed by physiotherapy. More recently reliance has been placed upon the injections, given—in the words of Mr. Grant Waugh—until he or the patient gets fed up. Surely the height of clinical optimism!

The acid treatment of arthritic joints has grown to huge proportions. It is somewhat reprehensible that an over-credulous profession has tended to accept and try it without more than empirical evidence, and that of an unconfirmed nature. We should retrace and confirm the evidence, and secure the scientific data which led to the trial of acid injection, or, failing or as well as this, we should undertake to produce adequate statistics of its value in a controlled series of cases.

In his articles Mr. Grant Waugh has hinted that periarticular may be as valuable as intra-articular injections. To date there appears to be no evidence that acid injection results in any prolonged alteration in synovial fluid *p*H, surely a necessary observation. Failing this data, any argument over the relative value of intra- and extra-articular injections must perforce be conjectural, as also must be any theoretical discussion of the whole problem.

The three cases of osteo-arthritis of the hip presented today have all had a fair trial of procaine lactic acid injections. Two of the subjects have expressed themselves as somewhat improved. This small series represents 25 injections, which have on occasion been combined with "diodone", an opaque dye, in order to ascertain where we deposited the solution. It is unfortunate that, owing to the difficulty of the procedure, only once in these 25 injections have we had radiographic proof that the solution was given into the required joint, and this in spite of the invaluable aid given to us by Mr. Hindenach, orthopaedic surgeon to the West London Hospital, who would, I think, agree that the injection of the arthritic hip joint is a difficult procedure. Why, then, choose this joint to help evaluate acid therapy? This has been done solely because it is the one joint which, when affected by arthritis, is resistant to most forms of treatment.

My experience, small as it is, has little significance in a review of the whole problem, but it does justify a few tentative conclusions, namely: (1) that the arthritic hip joint is not an easy target; (2) that the anterior approach, despite its apparent disadvantages, seems to be more accurate; (3) that the sensation of penetrating the capsule does not always indicate entry into the joint (there appear to be other structures capable of giving rise to the same sensation); (4) that asepsis is essential (this needs stressing in view of the vast number of cases being treated); (5) that a long needle, preferably six-inch, alone can offer any hope of reaching the joint by the anterior approach in an obese patient.

In my opinion these three patients have not had intra-articular injections, yet two report improvement which rightly or wrongly they are inclined to attribute to the injections. If this is so, then further thought is required to elucidate the morbid physiological and biochemical reactions which are taking place. The optimistic use of P.L.A. treatment all over the country demands that a more scientific approach be made toward this problem in particular, and toward osteo-arthritis in general.

Effects of Stellate Ganglion Injection in the Treatment of the Painful Shoulder

R. M. MASON

The treatment of so-called " frozen shoulder " by stellate ganglion block was suggested, as a result of a visit by Dr. Steinbrocker of New York, by Dr. Copeman. Steinbrocker had been favourably impressed with this method of treatment in cases of the shoulder-hand syndrome.

The technique was his. An anterior approach is used, the needle passing between the carotid artery and the trachea. 20 c.cm. of ½ per cent. procaine is inserted, and the production of a Horner's syndrome confirms that the stellate ganglion has been infiltrated. This may be repeated once or twice weekly as indicated.

A housewife, aged 61 years, had a painful disability of the right shoulder for twenty years, following an injury. All movements of that shoulder were painful and limited, but there were no other abnormal physical signs. Radiographs of the shoulder, hand, and cervical spine showed no abnormalities. The erythrocyte sedimentation rate was 11 mm. in the first hour (Westergren). The blood count was normal.

After three weeks of heat and exercises to the right shoulder she had regained full movement, but this remained painful. The right stellate ganglion was infiltrated with 20 c.cm. of ½ per cent. procaine in normal saline weekly for four weeks. A Horner's syndrome was produced on each occasion. Relief of symptoms increased with each treatment, until she was cured apart from residual tenderness at the deltoid insertion. On the fifth occasion penetration of an artery occurred, and no procaine was therefore inserted. For the next five days she complained of pain down her right arm, which ended suddenly with the appearance of " bruises " on the dorsum of her right hand. The shoulder remained satisfactory, with full painless movement.

No conclusions have yet been drawn as to the efficacy or otherwise of such treatment in this condition. The evidence as to the role of the sympathetic in pain conduction is conflicting. Nathan [1] suggests that, in causalgia from peripheral nerve lesions, the sympathetic carries efferent impulses which stimulate somatic sensory axons. He quotes the hypothesis of Lèriche who believes that the irritation of scar tissue sets up a continuous stimulus to a vasomotor reflex, and that the pain resulting from vasoconstriction keeps the vasoconstriction going, causing " une veritable maladie nouvelle "; sympathetic block thus relieves the pain by breaking the reflex arc restoring a normal vascular tone to the part. Doupe and others [2] suggest that the conjunction of sympathetic fibres and sensory fibres occurs at the periphery, and that ischaemia, or impaired nutrition, of the terminal nerves leads to defective insulation and cross-stimulation. Shaw [1] believed that sympathetic fibres carry impulses of pain, and that the anatomic sympathetic pathway in the cervico-thoracic region contains spinal sensory fibres; and Greenhill [2] suggests that the pelvic sympathetic carries afferent sensory fibres giving rise to pain.

Despite the lack of a firm theoretical basis it seems that this is a therapeutic measure worthy of trial in this type of case.

1 *Brain*, 1947, 70, 145.
2 *J. Neurol., Neurosurg., Psychiat.*, 1944, 7, 33.

Other Papers

Before Dr. Nicholson's paper, Dr. Oswald Savage described two cases of rheumatoid arthritis treated by Speransky's method. Dr. D. Preiskel also showed two cases, one of polycythaemia with gout, and one of pernicious anaemia with rheumatoid arthritis. Mr. J. C. R. Hindenach showed a case of osteo-arthritis of the hip treated by cup arthroplasty.

Compte-rendu de la Réunion de la " Heberden Society "

TENUE LES 17 ET 18 OCTOBRE 1947

La réunion commença par une communication sur la spondylite. Le Dr. C. W. Buckley pensait qu'il serait raisonnable d'insister sur le fait qu'on ne devrait pas poser un diagnostic de spondylite en se basant sur des modifications sacro-iliaques sauf lorsque le taux de sédimentation était augmenté de façon manifeste ou lorsqu'elles étaient accompagnées de modifications caractéristiques de la colonne vertébrale. Il était d'avis que l'opinion habituelle que la spondylite ankylosante est une simple arthrite rhumatismale touchant la colonne vertébrale a fortement contribué à retarder les progrès de son étude et à masquer quelques-uns de ses caractères les plus importants. Le Dr. Buckley passa en revue la littérature récente, y compris le travail de Davidson sur l'excrétion du 17-cétostéroïde dans la spondylite.

M. Norman Capener traita du traitement orthopédique de la spondylite ankylosante. Il insista sur la nécessité du repos physiologique, c'est-à-dire du repos maximum nécessaire pour le traitement, mais repos minimum pour obtenir une restoration fonctionnelle parfaite. Dans l'orthopédie préventive, le but était de donner des directives sur la technique du repos et son " dosage ". On peut souvent corriger la difformité par ostéotomie. L'idéal du point de vue chirurgical serait de rendre le mouvement sans douleur aux articulations ankylosées. On dispose de différents types d'arthroplastic de la hanche; lui-même n'a obtenu de résultats ayant quelque valeur que dans un seul cas par la méthode plus ancienne de l'arthroplastie par lambeau de fascia. Depuis la guerre il a fait de l'arthroplastie en utilisant la méthode Smith-Petersen, mais jusqu'à présent il ne pouvait savoir si les résultats seraient meilleurs. M. Capener souhaitait que les chirurgiens pulmonaires soient bientôt à même de décrire une technique d'arthroplastie costo-vertébrale.

1 *Arch. Surg.*, 1933, 27, 1072.
2 *Brit. med. J.*, 1947, 2, 859.

Le Dr. D. I. C. Williams décrivit les différents aspects de la ràdiothérapie dans la spondylite ankylosante: technique; indications; contre-indications; hasards et dangers; le " rationale " (a) pathologique, et (b) clinique; et les résultats d'un tel traitement. Il mentionna les dangers pour la peau et le sang et les organes génitaux ainsi que les réactions constitutionnelles. Il suggéra le plan de traitement suivant pour la spondylite ankylosante. Le premier temps est le traitement aux rayons *x*. A la fin du traitement le malade devrait être renvoyé dans le service d'orthopédie pour traitement correctif et surveillance, car le pronostic—compte tenu de l'époque à laquelle le diagnostic est fait et de l'efficacité du traitement par la radiothérapie—dépend énormément du traitement orthopédique du malade. Il devrait rester sous surveillance médicale pendant longtemps, et il peut être nécessaire d'intervenir à nouveau dans le cas où la douleur apparaîtrait en d'autres endroits. Cette communication fut suivie d'une discussion.

Les Drs. G. D. Kersley et M. H. L. Desmarais décrivirent l'anatomie pathologique et l'histologie des lésions rhumatismales dans le muscle et ailleurs. La formation de nodules dans l'arthrite rhumatismale était très similaire à celle que l'on constate dans certains cas de rhumatisme articulaire aigu, mais les lésions pouvaient être différenciées avec une grande certitude histologiquement. Parmi les caractéres distinctifs on notait la dimension de la zone nécrotique centrale, entourée d'une couche limitante de cellules mésenchymateuses disposées radialement, et elle-même entourée d'un stroma fibreux dans lequel on peut souvent voir des foyers lymphocytaires du type rhumatismal.

Le Dr. Bywaters parla des similitudes radiologiques entre l'arthrite rhumatismale et l'ostéo-arthropathie pulmonaire qui pourraient éclairer le mécanisme de cette dernière.

Le Dr. F. Bach parla de l'emploi de la pénicilline dans le traitement des rhumatismes aigu et chronique. Ses conclusions sont les suivantes:

1. La pénicilline n'a pas d'action certaine sur l'arthrite de type rhumatismal.

2. On a pensé depuis longtemps que l'infection est un facteur étiologique important.

3. L'association de l'arthrite rhumatismale et de la dilatation des bronches est assez fréquente, particulièrement chez les personnes d'âge mûr et les vieillards.

4. Dans la littérature on fait rarement mention ou pas du tout de la dilatation des bronches comme foyer d'infection dans l'arthrite rhumatismale.

5. Le traitement de la dilatation des bronches semble avoir un effet bienfaisant sur l'état général du malade, mais, jusqu'à présent, on n'a pas d'indications d'un effet favorable à long terme sur les manifestations arthritiques de l'arthrite rhumatismale.

6. La pénicilline ne doit pas être administrée sans discrimination car elle peut modifier les mécanismes de défense de l'organisme—comme cela a été démontré.

Le Dr. R. G. Abercrombie a décrit les symptomes secondaires suivants du déplacement des disques intervertébraux: le signe plantaire; le signe de " l'expiration forcée "; la verticalité de la colonne lombaire.

Le Dr. D. P. Nicholson discuta le traitement acidifiant de la hanche arthritique et conclut: (1) que la hanche n'est pas facile à atteindre; (2) que la voie d'abord antérieure, malgré ses inconvénients apparents, semble plus précise; (3) que le sensation d'avoir pénétré dans la capsule ne signifie pas toujours que l'on est effectivement entré dans l'articulation (il semble que d'autres structures soient susceptibles de donner lieu à une sensation analogue); (4) que l'asepsie est essentielle; (5) que seule une longue aiguille, de quinze centimètres de préférence, peut donner une chance d'atteindre l'articulation par la voie d'abord antérieure chez un malade obèse.

Le Dr. R. M. Mason décrivit les effets de l'infiltration du ganglion stellaire dans le traitement de la douleur de l'épaule. Il conclut que, en dépit du manque de base théorique ferme il semblait que c'était là une mesure thérapeutique digne d'être essayée dans certains cas.

AMERICAN RHEUMATISM ASSOCIATION

PROCEEDINGS OF THE ANNUAL MEETING, 1947

The Annual Meeting of the American Rheumatism Association was held in Atlantic City, New Jersey, on June 7, 1947. The Presidential Address was delivered by Dr. Walter Bauer, and this address, together with reports of all papers read at the meeting and discussions on them, is printed below.

PRESIDENTIAL ADDRESS

The Challenge of Adolescence

WALTER BAUER

The American Rheumatism Association is a young medical society. This year, 1947, marks its fifteenth birthday. Endocrinologically speaking, the society has reached the age of puberty. Its activities during the first fifteen years of life have been in accord with the purposes for which the society was conceived. Its record of accomplishment, despite the interruption of the war years, affords grounds for encouragement and legitimate hope of a successful adolescence. If the latter is achieved, we shall witness a maturity evidenced by marked scientific and clinical advancement in the fields of rheumatic and allied diseases. It is the adolescent phase of the society's development with which I wish to concern myself during this brief address.

The growth requirements during this period of adolescence are many. The most important of these are: a diversified and distinguished membership and adequate support of their research activities. The former is the responsibility of the Membership Committee; the latter, the obligation of the Committee on Research and Education. If the latter group recommends that our society embark on a national fund-raising campaign in order to provide needed financial support, it will be the duty of our membership to foster a vigorous educational, research, and care-of-the-patient programme.

I will not dwell on the first of these requisites—education—other than to remind you of the Hippocratic oath which reads, "I will impart this art by precept, by lecture, and by every mode of teaching."

The need for both clinical and basic research in the field of rheumatic diseases is ever evident. Time will not permit an adequate presentation of this second requisite. It will suffice to state that the search for specific remedies has led nowhere. Some will accuse me of medical nihilism if I express my views on this subject by modifying slightly the classic observation by Oliver Wendell Holmes: "If most of the so-called specific rheumatic medicines were thrown into the Atlantic ocean, it would be much better for mankind and so much worse for the fishes."

Through accurate clinical studies, we can advance our knowledge of the natural history of the rheumatic and allied diseases and also determine the type of bodily changes which ensue.

The urgency for basic research is, I am sure, obvious to all students of rheumatic diseases. This will necessitate a better definition of pathogenesis, and the mechanisms involved will remain unchanged. Such definition of tissue, both normal and diseased, will require the employment of the newer techniques introduced by the histochemist, the physical chemist, and those interested in molecular structure. To cite but one example, until such an approach is undertaken we will not know why tissues high in mucin content are predominantly involved in rheumatoid arthritis.

Adequate care of the patient will always be an absolute requisite of the members of this society. This being the case, we must make use of every known preventive and curative measure for communities as well as for individuals. The need for the former is especially great. Such community programmes of care should be the responsibility of the affiliated groups and should also include convalescence and rehabilitation.

It is also essential that the student of rheumatic diseases understand the reaction to illness. "He must be familiar not only with the personality involved, but also with certain psychological concepts related to disability. Thus, attention must be directed not only to the degree of structural impairment, but also to the personality as it relates to past capacities and flexibilities, as well as to its means of adapting to the specific disability. The emotional setting of the illness, the special meaning of the disability to the individual, and the past and present means used by the individual to manage or handle anxiety mobilized by disability, require particular attention. Of equal importance is the character of the medical attention. Many individuals are harmed

through the use of repetitive and unnecessary diagnostic procedures which in many instances reinforce certain basic emotional patterns. Last, but not least, the emotional capacity of the physician to deal with disabled people without adopting hostile attitudes is of primary importance in any therapeutic programme."

I sincerely hope that this society will not sponsor an American board for physicians interested in rheumatic diseases. The folly of such, I am sure, is apparent to some of you. I also hope that if special clinics or units for the study of rheumatic diseases are established, they will become, wherever possible, an integral part of large, general hospitals and not isolated institutions. In my opinion, the latter are very likely to suffer from the lack of stimulus obtained from the other departments of a general hospital.

I fully appreciate that the foregoing account of the requisites for a successful adolescence and maturity of our society have been presented all too briefly. However, the detailed requirements can be supplied as we move upward on the growth curve. As we proceed forward, we must be ever mindful that the contributions of a society reflect the attitudes and activities of its membership.

SYMPOSIUM ON COLLAGEN

Electron Microscope Study of the Structure of Connective Tissue

JEROME GROSS

The fine structure of collagen has been the subject of intensive research in the Department of Biology at the Massachusetts Institute of Technology for the past five years. Electron microscopy and *x*-ray diffraction studies have contributed considerable information concerning the submicroscopic architecture of this fibrous protein. Schmitt and others [1] demonstrated with the electron microscope the presence of an axial periodicity of 640 Ångstrom units between electron dense and light bonds in the collagen fibrils. This figure coincided exactly with the spacing previously determined by Bear [2] of this laboratory using *x*-ray diffraction. Staining the collagen fibril with phosphotungstic acid revealed at least five sub-periods within the larger period. Shadow casting has demonstrated the presence of contour discontinuities of the same periodicity. This general pattern has been observed in collagen of fish, amphibia, and various mammals including man. It is also present in the collagen of all tissues examined thus far.

Schmitt and others showed the presence of longitudinal cleavage planes in the collagen fibril and demonstrated the same axial periodicity in the component sub-fibrils. Swelling in dilute acid will cleave the fibrils to filaments of the order of 100 Ångstrom units in width, which are readily visualized when shadowed. The fine structure of these filaments and the nature of the cross-striations in the larger fibrils are being studied intensively.

Because of the close association of the acid polysaccharides, hyaluronic acid, and chondroitin sulphate with connective tissue, their occurrence in other structures such as cartilage, vitreous humour, cornea, umbilical cord, synovial fluid, and some tumours, an investigation of these substances is now under way. Electron micrographs of hyaluronate reveal fibrous patterns which reflect the degree and possibly the form of polymerization.

It is believed that the elucidation of the structure of collagen and associated substances may promise a basis for understanding some of the pathological changes which occur in connective tissue.

Cement Substances of Connective Tissue

KARL MEYER

Histologically two types of interfibrillar material have been distinguished: first, the amorphous and viscous ground substance; and secondly, the metachromatically-staining cement substances proper which are supposed to form a fine sheath around the individual fibrils. Both types of interfibrillar substances consist mainly of proteins and mucopolysaccharides. While the nature of the proteins is unknown, the mucopolysaccharides have been characterized, at least in some connective tissues, as hyaluronic acid and as a chondroitin sulphate. Hyaluronic acid, a polymer of acetylglucosamine and glucuronic acid, has a molecular weight of 200 to 500,000 and more, and has been isolated from mesodermal tissues, vitreous, and synovial fluid, and group A streptococci. The enzyme depolymerizing and hydrolyzing hyaluronic acid has been named hyaluronidase; it is the cause of the "spreading reaction" in the skin.

Chondroitin sulphates, polymers of acetylgalactosamine-sulphate and glucuronic acid, have likewise molecular weights of several hundred thousand. In contrast to hyaluronic acid they may have branched chains. The protein complexes of chondroitin sulphates are more stable than those of hyaluronate, forming in some tissues at least stable compounds, while hyaluronic acid forms only polar complexes with proteins which are easily dissociated.

[1] *J. cell. comp. Physiol.*, 1942, **20**, 11.
[2] *J. Amer. chem. Soc.*, 1942, **64**, 727.

Synovial fluid seems to be formed partly by dialysis and partly by secretion. The viscosity of the fluid is practically due only to hyaluronic acid. By a turbidimetric method normal and pathological fluids were compared, and the normal showed greater viscosities but lower hyaluronic acid concentrations. Furthermore, hyaluronic acid of pathological fluids precipitates with acidified protein, forming a stable turbidity, while that of normal fluids precipitates as fibres. The fibre formation is prevented by previous incubation with 1/100 of a unit of hyaluronidase. Whether the difference in degree of polymerization between normal and pathological fluids is due to hyaluronidase activity is not known at present.

The chemistry of connective tissue may be correlated with the histology if we assume that the amorphous ground substance contains hyaluronic acid while the cement substances contain different chondroitin sulphates as their typical components.

Lesions Resulting from Albumin and Globulin Injections

C. v. Z. HAWN

1. Groups of normal rabbits were given single intravenous injections of foreign proteins in doses of 1 g. per kilo, bled at regular intervals for serologic studies, and sacrificed after varying lengths of time for pathological studies. The protein solutions used were of crystallized bovine serum albumin, bovine serum gamma globulin, and bovine serum. The experiments were planned, first, to correlate the sequence of pathological and immunological changes, and second, to compare the responses to two chemically and immunologically distinct plasma protein fractions and to the whole serum of the same species.

2. (*a*) The principal pathological lesions in rabbits given bovine serum were similar to those which have been previously observed following the injection of horse serum and were characterized by widely dispersed but segmental acute inflammatory lesions of the arteries. These lesions were at their height two weeks after injection and showed marked repair at four weeks. (*b*) Crystallized bovine serum albumin produced lesions almost exclusively confined to the arteries, which were at their height at two weeks, were healing at three, and healed by four weeks. The lesions were less numerous and less intense than in animals given whole serum and were only found in some of the animals. (*c*) Bovine serum gamma globulin elicited quite different histologic sequences. The most striking lesions involved the glomeruli of the kidneys, and to a lesser degree, the heart. Lesions in the liver and joints were present but less conspicuous, and arterial lesions were rare and slight in degree. The lesions not only differed from those in rabbits given albumin in distribution but in timing, since they were most widespread and acute at one week and were healing at two weeks after injection. Moreover, lesions were observed in almost every animal.

3. Results of immunological studies were consistent with the interpretation that the pathological lesions were due to an antigen-antibody reaction in the tissues, as shown by the following: (*a*) acute lesions were observed only when antigen was present and before antibody appeared in the circulation. (*b*) healing of lesions was observed (with one exception) only when antigen had almost or completely disappeared from the circulation, usually with the appearance of antibody; (*c*) there was a correlation between the rapidity of evolution of the lesions and the rapidity with which the antigen disappeared from the circulation; (*d*) there was a rough correlation between the proportion of animals showing lesions and the proportion developing antibodies after the injection of a particular protein solution.

(Illustrations to this paper were shown.)

The "Pararheumatic Diseases"

PAUL KLEMPERER

It is generally accepted that the morbid anatomy of rheumatic fever is characterized by a more or less systemic involvement of the connective tissues. This involvement becomes first evident as fibrinoid alteration of the collagen fibres and swelling of the homogeneous ground substance. It is followed by cellular proliferation which, especially in the heart, assumes the characteristic form of Aschoff nodules. Because of the absence of demonstrable pathogenic organisms, Klinge assumed that the tissue damage in rheumatic fever was determined by hypersensitivity of the host. The occurrence of similar connective-tissue changes in experimental local anaphylaxis seems to lend support to this hypothesis. The observations of striking fibrinoid alterations of the vasculature suggested to Klinge a similar pathogenesis for periarteritis nodosa, malignant sclerosis, and thromboangiitis obliterans. Because of the presence of widespread identical connective-tissue lesions in acute lupus erythematosus and scleroderma these diseases were also included within the group of maladies with an allergic background. Roessle proposed that "the old designation, rheumatic, should yield to the new wider concept of allergic diseases". Theilum, accepting the haemolytic streptococcus as the cause of rheumatic fever, suggested the term "pararheumatic" to indicate the possible difference in specific aetiology of the

various other members of the group of diseases with a common pathogenetic background of allergy.

In our studies of acute lupus erythematosus and generalized scleroderma, Baehr, Schifrin, Pollack, and I were also impressed by the frequent widespread implication of the connective tissue. We were fully aware of the possible significance of allergy in the causation of fibrinoid collagen alteration; but we were hesitant to accept this aetiology because of these histological features only, especially since classical manifestations of allergy are absent in the clinical course of these diseases. Moreover, we were cognizant of the fact that collagen alterations identical with or hardly distinguishable from those seen in allergy can be produced experimentally by various factors. More fundamental information regarding the nature and cause of the fibrinoid alteration of the collagen fibres is necessary before we can approach the problem of the aetiology of human disease characterized by diffuse collagen changes.

Discussion on Symposium on Collagen

DR. CHARLES RAGAN (New York): We have been interested in the hyaluronic-acid content of joint fluid for about five years, and the implications of what we have found still need explanation; however, we have observed, on tapping knee joints post mortem, that normal human fluid is very viscous, much more viscous than any pathological fluids. We have obtained fluid from patients with rheumatoid arthritis, osteo-arthritis, and rheumatic fever. A small amount of fluid is obtained from a normal joint, and the viscosity is difficult to measure in such small amounts of fluids. We have had to approximate it by dilution curves, but we feel that the results are accurate enough to say that the viscosity of normal fluids is very high. However, the hyaluronic acid content is not much greater, which would mean that in normal fluids the hyaluronate is in a more or less polymerized state. We have evidence that in the abnormal states the hyaluronic acid has been depolymerized to some extent. This has been obtained by plotting the viscosity on the ordinate and the concentration of hyaluronic acid on the abscissa. On such a curve, similar to the dilution curve, normal fluids appear to the left, which would indicate that the abnormal fluids have been exposed to some hyaluronidase. These fluids, when standing at icebox temperature, if kept sterile, do not change in viscosity, which would indicate that no hyaluronidase is present.

Speaking as a clinician, I think we are almost convinced that rheumatoid arthritis is a disease of hypersensitivity, but we still do not know what the antigen is, or how to approach the disease from this angle.

DR. MARIAN W. ROPES (Boston, Massachusetts): We also have been very much interested in the hyaluronic acid content of joint fluids for about fifteen years and have found similarly that the normal viscosity is very high, while the relative concentration of the hyaluronic acid-protein compound is not very high. In fluids from joint diseases there is considerable variation. In the rheumatoid fluids we find a comparatively low concentration of hyaluronate per unit volume with low viscosity, much lower than normal fluid. In rheumatic fever we find relatively little change from normal in the viscosity per unit concentration, and in disseminated lupus we find viscosities in the range of normal fluids, and sometimes an actually higher than normal concentration of mucin per unit volume. We have attempted to correlate the breakdown of hyaluronic acid in rheumatoid fluids by comparing the log of the viscosity with the square root of the concentration of the glucosamine of the hyaluronic acid. This gives a straight-line relationship in normal fluid. We have attempted to use this relationship as evidence of the degree of breakdown of hyaluronate, but it has not been consistent in all fluids. We still feel it is impossible to say whether or not the change in hyaluronic acid in rheumatoid arthritis is due to a breakdown or to inadequate synthesis due to the lack, possibly, of the proper enzyme. We have been unable to find hyaluronidase activity in sterile normal joint fluid or in fluid from any joint disease that we have tested. Also, we have tried to demonstrate it in normal and abnormal synovial membranes, but if the preparations remain sterile we have found no hyaluronidase activity.

Has Dr. Klemperer been able to obtain metachromatic staining with toluidine blue from isolated compounds that do not contain sulphate? In our experience to date we have not been able to do so.

DR. RICHARD H. FREYBERG (New York): I should like to ask Dr. Gross whether studies have been done or are being contemplated with electron microscopy of abnormal connective-tissue fibres.

Dr. Meyer's presentation was of great interest to me. Many of us have felt that the histologic changes and many clinical problems of rheumatoid arthritis are probably due to antigenic or enzymatic changes. The studies Dr. Meyer has done certainly open the door for us to make reasonable explanation for some abnormalities of connective tissue on the basis of either immunologic or enzymatic alterations.

The acute lesions that Dr. Hawn showed in his excellent illustrations, that result from a single injection of albumin, indicate how extensive is the effect and damage from such a single insult. Repeated insults and the continuity of resulting abnormalities going on in a chronic disease such as rheumatoid arthritis, would reasonably explain the mixture of changes of developing and advancing disease, together with healing and scarring which constitute the pathological picture that we see and which we should like to know more about from the functional standpoint.

Does Dr. Hawn have explanation for the different speeds of decrease of the albumin and globulin from the blood stream? Is this phenomenon related to differences in molecular weight? Has he studied the effect of proteins other than normal albumin, globulin, or serum injected into animals? Do similar pathologic changes result from the injection of digestion products of serum, or albumin, or from different proteinates?

We should all give serious thought to the papers of this symposium, to stimulate related studies which are so badly needed.

DR. WILLIAM D. ROBINSON (Ann Arbor, Michigan): I wish to ask Dr. Meyer if there is any evidence that alterations in the sedimentation rate (admittedly a non-specific manifestation) are in any way related to change in concentration or the physical characteristics of the glycoproteins. I should like to ask Dr. Hawn how consistently the lesions which he described were produced in rabbits and whether there is any correlation between the rate of antibody formation and the appearance of these lesions. I also wish to call attention to the fact that the lesions produced by the injection of normal protein derivatives were acute lesions. While that may be analogous to those seen in rheumatic fever, they do not appear related to the chronic proliferating lesions which we see in rheumatoid arthritis.

DR. JOHN R. PAUL (New Haven, Connecticut): How much are we dealing with non-specific changes, and to what extent do these changes, of which we have seen so many examples, have to do with rheumatic fever and rheumatoid arthritis?

Dr. Meyer spoke of substances inhibitory to hyaluronidase. We have been interested in our laboratory in some work by Friou and Wenner,[1] indicating that in patients with rheumatic fever there was an increase, not striking but definite, of an "anti-hyaluronidase substance" in the blood stream, and there was a moderate increase in patients with haemolytic streptococcal infections. Does Dr. Meyer have any possible explanation for this finding in rheumatic fever?

DR. DAVID H. KLING (Los Angeles, California): Does Dr. Meyer accept the conception of the dual nature of synovial effusions; one fraction being a dialysate from the blood, and the other produced by secretion of special cells in the synovial membrane?

DR. RUSSELL L. CECIL (New York): Is a collagen fibre a part of the connective-tissue cell? How does fibrinoid degeneration differ from old-fashioned hyalin degeneration? I get the impression that the fibrinoid degeneration, while an interesting phenomenon, is almost universally found in chronic inflammatory and degenerative tissue.

DR. WALTER BAUER (Boston, Massachusetts): Will Dr. Hawn tell us what type of lesion he observed when he employed small doses of albumin and globulin? Has Dr. Gross noted any appreciable difference in the collagen of the newborn as compared to that of the aged? Would Dr. Meyer tell us more about the synthesis and breakdown of hyaluronic acid, even at the expense of postulation? Can Dr. Klemperer explain the differences in cellular response which we observe in these diseases? For instance, the cellular response seen in serous cavities in lupus erythematosus may differ greatly from that seen in some of the allied diseases. Would he comment on the specificity of these collagen lesions? How does he observe them in other diseases? Has he seen cases that present the classical findings of lupus erythematosus disseminatus and yet at autopsy are found to have the characteristic lesion of periarteritis nodosa? If so, how does he interpret them?

[1] *J. infect. Dis.*, 1947, **80**, 185.

DR. FRANCISCO P. MIRANDA (Mexico City): I should like to say a few words about the work of Dr. Guerra, in Mexico, on the question of the possible explanation of salicylate action of hyaluronidase. He has been using Evans's blue as a detector of the spreading factor, showing by measurement of the area of spreading of Evans's blue in the connective tissue the relative spreading factor in different patients, and he has found that rheumatic patients form one of the groups of those who have great spreading tendency in their connective tissue.

In Mexico we are convinced of the importance of connective-tissue lesions. Dr. Perrin and Dr. Evaro have been studying patients with rheumatic fever, and cadavers of patients dying from rheumatic fever, and have found a very constant lesion in the periosteum, so that these lesions can be proved to be of rheumatic fever origin. There have also been others working on this in Mexico. In this connexion I should like to ask Dr. Meyer and Dr. Hawn what is the relative quantity of lymphocytes and polymorphonuclear leucocytes they find in inflammatory reactions? This question is important, to my mind, because the question of the place of antigen formation is now believed to be within the lymphocytes rather than other cells. There are two steps in the question of the relation of antigen and antibody: first, the production within the cells of these antibodies; and, secondly, the liberation of these antibodies by the destruction of the lymphocytic cell, which is probably initiated by the action of corticotropic hormone. These relations can be found in the question of the velocity of the disappearance of lymphocytes from the site of the reaction.

CLOSING DISCUSSION OF SYMPOSIUM ON COLLAGEN

DR. JEROME GROSS (Cambridge, Massachusetts): Dr. Freyberg asked whether or not we are studying abnormal connective tissue. We have felt the need of learning a great deal more about the normal before we felt competent to handle abnormal material. There is considerable variation in what can be observed in normal connective tissue depending on its source and the method of preparation for electron microscopy. Therefore a knowledge of the effect of various procedures is necessary before the identification of pathological changes is possible. The study of abnormal connective tissue is contemplated as soon as we feel sufficiently informed about the normal state.

Dr. Bauer wanted to know whether we had found any difference between the connective tissues of young and old. The first human material I had an opportunity to examine came from the skins of a seven-month-old premature and an eighty-nine-year-old gentleman. The baby's collagen was embedded in masses of gelatinous material which was not easily separated, which made it very difficult to obtain clean enough fibres. On the other hand the old man's collagen was very easy to clean and showed considerable fine structure. This important problem is also slated for future study.

DR. KARL MEYER (New York): The first question was about erythrocyte sedimentation rate in rheumatic fever and rheumatoid arthritis and its relation to hyaluronic

acid. A few years ago we published a paper in which it was shown that intravenously injected highly polymerized hyaluronate in guinea-pig and rabbit caused a marked increase in the erythrocyte sedimentation rate (ESR), which disappeared promptly after intravenous injection of hyaluronidase. It was further found, but not published in detail, that purified testicular extracts abolished *in vitro* the elevated ESR of rheumatic fever patients in 100 per cent., and of rheumatoid arthritis patients in 50 per cent. of the cases. However, this effect was later shown not to be due to the hyaluronidase contained in the testicular extracts, but to an enzymatic action on some component of the stroma, as Dr. Ragan has shown. What this component is we do not know. The ESR-increasing effect of hyaluronic acid is a property common to all high polymer linear colloids, regardless of their chemical nature. It might be suspected that in rheumatic diseases such linear colloids of connective tissue enter the blood stream.

Dr. Paul's question was whether we had any information on hyaluronidase inhibition in rheumatic fever and haemolytic streptococcus infections. The test for inhibitory action on hyaluronidase is complicated, since it depends on the purity of both the enzyme and the substrate and on the salts present. Under certain experimental conditions, for example, heparin has been shown to be a very powerful inhibitor of hyaluronidase. We have shown that hyaluronic acid samples, especially those from umbilical cord, may contain potent inhibitors of hyaluronidase; these inhibitors can be removed from the hyaluronate.

Group A haemolytic streptococci, however, do contain a very powerful inhibitor of hyaluronidase, which seems quite different in nature from the inhibitors found in serum and tissues. The study of the latter seems to me very much worth while.

As to the question of Dr. Kling, we believe in the dual nature of the origin of synovial fluid, namely, that part of the fluid is formed by dialysis, especially most of the water and diffusible elements; but that part of it, especially the hyaluronate, is formed by a secretory process requiring energy-producing reactions.

The question of Dr. Bauer about breakdown and synthesis of hyaluronic acid is one of the most fundamental problems for which we would like to know the answer. We do not know with certainty which cells produce hyaluronic acid. We suspect that fibroblasts do the synthesis. Then the question arises whether or not the same cells of the dermis or of the umbilical cord synthesize chondroitin sulphuric acid beside hyaluronic acid. We feel quite certain that hyaluronidase has no synthetic function, that is, synthesis and breakdown take completely different pathways as, for example, in glycogen. It seems at the present time that the synthesis is very complex. The synthesis of the basic disaccharide unit probably takes place in the liver. These circulating disaccharides may then be polymerized by mesodermal cells into the final polysacccharides.

The breakdown of hyaluronic acid is simpler but is also due to a number of enzymes which have not yet been separated. The difficulty here is the absence of well-defined substrates, which may have to be synthesized.

DR. C. V. Z. HAWN (Boston, Massachusetts): In answer to the first question, I know of no simple explanation of the observed difference in the rates of disappearance from the circulation of the injected albumin and gamma globulin. I think it would be naive to explain the difference only on the basis of molecular size, shape, or weight. The observed difference merely poses a problem rather than answers one.

We have not yet investigated antigens other than these supposedly normal proteins. We hope in the future to use proteins which have been chemically altered. These may provide more useful information than the native proteins alone.

There was a question raised as to the frequency and consistency of these observed lesions and the correlation with the rate of disappearance of antigen and the formation of antibodies. There was a correlation between the rapidity of evolution of the lesions and the rapidity with which the antigen disappeared from the circulation. There was also a correlation between the proportion of animals showing lesions and the proportion developing antibodies after the injection of a particular protein solution.

I am well aware of the fact that I have described only the evolution and repair of acute lesions. As Dr. Klemperer has emphasized, the tissues can react in only a few established patterns of sequences to a large number of different noxious stimuli. It would be fallacious to accept these experimentally produced lesions as the counterparts of clinical disease entities. However, there is experimental evidence from other investigators that chronic diseases, particularly nephritis, may result under the conditions of certain experiments dealing with *in vivo* union of antigen and antibody. The speculation seems justified that when antigens are used which are chemically far different from the experimental animal's own substances, the mechanism for the removal of these may be more complicated than that with simple heterologous proteins, and more complicated histological sequences may result.

In answer to Dr. Bauer, we have not systematically investigated the amount of antigen required for the production of these lesions. The described amount, 1 g. per kilo of body weight, was first tried when we were investigating the possible use of crystallized bovine albumin as a blood substitute in treatment of shock during the war. Inasmuch as an experimentally reproducible disease in some of the rabbits was observed after such injections, we have arbitrarily adhered to the original amounts of protein for these preliminary investigations. I doubt whether such a large injection is necessary, since I have seen several isolated instances in other experiments where much smaller amounts of antigen elicited comparable lesions.

The character of the cell exudate is a problem of great interest. I think the earliest lesions we have seen have been infiltrated by lymphocytes and monocytes. The polymorphonuclear leucocytes appear in large numbers after the lesion is already established, and in the milder lesions they are often absent. We are at present investigating the possibility of preventing lesions by depression of the lymphocytic series by various means.

DR. PAUL KLEMPERER (New York): Regarding the question on metachromasia and other muco-polysaccharides, it has been claimed that toluidine blue metachromasia is characteristic for sulphuric acid esters of high molecular weight. I am not quite able to support this statement because in the umbilical cord, which contains a great deal of polysaccharides, some metachromatic material is found that differs in its colour from that of typical metachromasia; this might well be hyaluronic acid. Unfortunately, there are not yet available reliable methods for mesenchymal mucus other than the one of toluidine blue metachromasia. There is a recent histochemical method for hyaluronic acid, but so far it has not given me satisfactory results.

I think today histologists are more or less agreed that the collagen fibre is no part of the cytoplasm of the fibroblast. I do not want to enter into the whole problem of fibre formation. I believe, in view of the original histologic investigations, the tissue culture experiments, and especially Wolbach and Howe's research in scurvy, that the collagen fibre develops from the homogeneous ground substance. Of course, the ground substance most likely derives from the fibroblasts, although the mechanism of its production still awaits further investigation. It would be interesting to repeat the experiments of Wolbach and Howe, to see whether the droplets within and outside the fibroblasts in scurvy are mucopolysaccharides.

Regarding the relation of hyaline to fibrinoid, hyaline is a purely descriptive term and does not denote more than a substance which is homogeneous and eosinophilic. According to this definition, fibrinoid would belong to the general group of connective-tissue hyaline. Differentiation of the hyaline substances is possible with the conventional methods of histology. Fibrinoid stains like fibrin, while other connective-tissue hyaline stains like collagen and has the *x*-ray diffraction pattern of collagen. I think I indicated in my remarks that the further analysis of the so-called fibrinoid alteration of the collagen fibre is of importance. I avoid speaking of fibrinoid "degeneration" because I do not know whether we should apply this term to alterations of an extracellular substance.

The cellular response in various diseases of the collagen tissue is a fundamental question. So far we can only say that there are definite differences in the cellular response. If one has the opportunity to examine early lesions in lupus erythematosus with fibrinoid alteration of the collagen tissue of the myocardium, one finds proliferation of fixed connective-tissue cells; but one never sees in lupus that conspicuous and characteristic differentiation into Aschoff cells seen in rheumatic fever. The cells evidently respond to the injury of the extracellular substances; they proliferate, but rapidly decay. One has to stress these subtle differences because they point to a possible fundamental difference in the pathogenesis of these two diseases. I think the question touches also upon the low white cell count in lupus erythematosus. However, I do not know the reason for the suppression of leucopoiesis, because this is a problem that is not answered by morphologic investigation of the bone marrow. It might be pointed out that if a patient with lupus erythematosus develops a secondary infection, such as cerebrospinal meningitis, the white cell count goes up.

Regarding the question of the specificity of collagen tissue lesions, I do not think that fibrinoid alteration should be considered specific. It is, however, of great importance because its presence is of diagnostic assistance in the individual case, and beyond that it has stimulated further inquiry. I think one must distinguish between two aspects of anatomic pathologic investigation. On the one hand it aims at establishing a diagnosis; this is interesting and important for the pathologist and helpful for the clinician. However, the ultimate object of anatomic pathology is to determine the fundamental nature of manifestations of disease as expressed in morphologic alterations.

Like other investigators, we also have found fibrinoid alterations in the affected vasculature in periarteritis nodosa; but in other sites, except for the valvular endocardium, it is not as common as in lupus erythematosus. In periarteritis nodosa and in rheumatic fever with striking vascular implication, glomerular lesions of the type seen in lupus erythematosus are not present. There is one alteration to which we paid little attention in our report in 1941, namely, the swelling of the connective-tissue ground substance. This, I believe, is a significant feature of the morbid picture and should be further investigated.

Typical periarteritic vascular lesions were found in only one of our cases of acute lupus erythematosus. This was an old case, records of which were kept in the files of our laboratory for some time before I came to the hospital. I cannot deny that the vascular changes were those of classical periarteritis nodosa.

OTHER PAPERS

Rheumatic Patients in the Armed Forces

MAY G. WILSON, JOAN W. PAYSON, and ROSE LUBSCHEZ

Two hundred and sixty-eight patients under medical supervision in the Children's Cardiac Clinic were of military age. Two-thirds volunteered or were drafted; one-third were rejected. The above authors presented the previous rheumatic history and degree of cardiac damage of 242 servicemen and rejectees. The distribution of the men in various services, military installations, and overseas theatres was given. A comparison of the morbidity among the men was presented for 400 patient years of experience in each group. The incidence of rheumatic fever was no greater than expected in civilian life. The reported high incidence of rheumatic fever in the World War 1939–45 was discussed. Data obtained from the Office of the Surgeon General, Selective Service Headquarters, and other sources, was analysed. Since data about the number of rheumatic susceptibles inducted were non-existent, it was assumed—on the basis of clinical experience—

that about two-thirds of the rheumatic susceptibles who presented themselves were inducted. By applying the civilian recurrence rate of 4 per cent. to an estimated pool of rheumatic subjects in service, the number of recurrent attacks of rheumatic fever which should have been observed in the armed services was estimated. Except for the Navy data, there was close agreement between the number of rheumatic recurrences expected and the number of attacks of rheumatic fever reported. It was concluded that most of the reported attacks of rheumatic fever in the armed services were recurrent attacks, and that the risk for recurrent attacks of rheumatic fever was no greater in the services than in civilian pursuits.

Discussion

DR. R. L. WARE (Bureau of Medicine and Surgery, U.S. Navy, Washington, D.C.): Dr. Wilson's paper is interesting from the Navy viewpoint in that it highlights one of the major problems that we experienced during the war years. Rheumatic fever has to be considered among the top eight or ten conditions in importance to the Navy during the war. It ranked fourth among all diseases and non-combat injuries as a cause of sick days, and it ranked fifteenth as a cause of separation from the service by medical discharge.

The Medical Department of the Navy has recognized the importance of rheumatic fever in the service by setting up special treatment centres and by assigning research units to conduct studies of the disease. In the Division of Medical Statistics we are undertaking a statistical study of the 21,000 cases of rheumatic fever that occurred in the Navy during the war. We are interested in knowing whether local climate influenced the development of rheumatic fever. We are also interested in determining what effect, if any, the state from which a man came may have had upon his developing the disease. We will also examine the association of incidence rates for streptococcal disease, as exemplified by scarlet fever, with the rate for rheumatic fever; and, in individual patients, the relationship of an attack of rheumatic fever to a preceding attack of scarlet fever. It is believed that the data under study may yield interesting information on these and other related aspects of the disease.

DR. ELVIRA M. DELIEE (New York): Dr. Wilson has had the enviable opportunity of following a large group of rheumatic children through adolescence into adult life and the armed forces. The great advantage which her patients have had, as I see it, is the opportunity for accurate diagnosis and uniform observation prior to military service. I am certain that a large proportion of recruits did not have the benefit of similar long-term supervision. Also, many who had rheumatic disease were totally unaware of its existence, physical signs in the heart either being absent or having regressed.

I should like to make a plea for the development of rheumatic fever registers in communities where appropriate diagnostic and supervisory facilities are available. The rheumatic fever problem is essentially a community responsibility because the disease is most prevalent in the low income groups. Furthermore, since the disease most commonly has its onset in children of school age, the rheumatic fever problem is, of necessity, closely integrated with the school health programme.

Recently, using the methods employed previously by Paul, I had the opportunity to conduct a school survey in the Lower East Side District of New York City. This survey was conducted with Dr. Charles Connor and Dr. Mortimer Weber, of New York University College of Medicine: 1,190 eighth grade children* were examined. Thirty-nine, or 3·3 per cent. of these children, were found to have existing or potential rheumatic heart disease. In addition, seven children were on home instruction or in special convalescent facilities, so that the incidence of rheumatic fever in these eighth grade children was nearer 4·0 per cent. It was found that thirteen, or one-third of these children were unknown to the School Health Service as having rheumatic disease. Five were totally unaware of the existence of their rheumatic disease. Conversely, four children had been wrongly diagnosed as having rheumatic heart disease. This state of confusion is well known to others who have made school surveys for rheumatic disease. A rheumatic fever register with cumulative evidence on each rheumatic child, based on accurate and verified diagnoses, would contribute materially to the solution of this problem. The register, furthermore, would serve as the basis for an organized community effort for the study and control of rheumatic fever.

Cardiac Changes in Rheumatoid Arthritis

WILLIAM S. CLARK and WALTER BAUER

Cardiac abnormalities were studied in a group of forty-five patients with definite rheumatoid arthritis on whom autopsies had been performed. The average age of the group at the time of death was fifty-one years and the average duration of the disease was twelve years. The diagnosis of rheumatoid arthritis was substantiated by typical clinical *x*-ray and histological findings. In all but two instances, no evidence of previous episodes of rheumatic fever could be demonstrated. In reviewing the clinical histories it was found that 50 per cent. of the patients had had evidence of heart disease before death. It was considered that hypertension and/or arteriosclerosis had been concerned in the aetiology in 50 per cent. of these, and rheumatic fever in 30 per cent. There were six instances of pericarditis. Seven patients had evidence of valvular disease. Mitral stenosis was demonstrable in five cases. At autopsy, atherosclerosis of the aorta and coronary arteries, usually with degenerative changes of the myocardium, was a rather constant finding. Focal myocarditis without definite histological evidence of rheumatic carditis was found in 16 per cent. of the

* The eighth grade corresponds to about the fourth form and is for children of about thirteen years of age.—Editor.

total group. Pericarditis was found in 44 per cent. Twenty per cent. had some degree of valvulitis, which had resulted in mitral stenosis in fourteen of the total group. A definite diagnosis of rheumatic heart disease could be made in but one instance. A peculiar aortitis and aortic valvulitis with pannus formation was observed in one heart. In two hearts there were nodules indistinguishable from the subcutaneous nodules of rheumatoid arthritis. The cardiac findings in this group suggested the possibility that involvement of the heart might be a systemic manifestation of rheumatoid arthritis.

Discussion

DR. EDWARD F. ROSENBERG (Chicago): Four years have elapsed since Dr. Baggenstoss and I reported the finding of a high incidence of rheumatic cardiac lesions in twenty-five individuals dying with rheumatoid arthritis. During this period developments regarding this observation have been most puzzling. Within a relatively short period reports from the University of Minnesota, from Montefiore Hospital in New York City, and from Yale University indicated that a high incidence of rheumatic cardiac lesions had likewise been discovered in series of autopsied cases of rheumatoid arthritis studied in those institutions. Dr. J. L. Hollander, of the University of Pennsylvania, told me recently that the series being studied under his direction is disclosing a similarly high incidence of rheumatic carditis.

This weighty evidence of the presence of inflammatory cardiac lesions in patients dying with rheumatoid arthritis is at variance with our observations regarding the condition of the heart in the living patient. Last year, with Drs. Weintraub, Bishop, and Hench, I reported that our earnest efforts to find rheumatic heart disease in a series of 150 cases had shown this incidence to be approximately 3 per cent.—about the same incidence as in a control series. Today we have heard Drs. Clark and Bauer report that the incidence of rheumatic heart disease was not high in their autopsied series.

All this indicates that the problem needs much more study. I have noted a recent tendency on the part of some cardiologists to teach that patients with rheumatoid arthritis often develop serious rheumatic heart disease. This may be the case, but we are not yet certain.

Family Incidence of Rheumatoid Spondylitis

BERNARD ROGOFF and R. H. FREYBERG

The families of 114 patients with rheumatoid spondylitis were carefully investigated to determine the family incidence of this disease. By careful history thirty-one patients revealed that other members of their family suffered with back disability. Eighteen of these families were personally examined, and ten (9 per cent.) were found to contain multiple cases of spondylitis. In one family three brothers and the father were found to suffer with spondylitis; in another, identical twins age 20 revealed bilateral sacro-iliac arthritis. In the thirteen unexamined families another 4 per cent. could be anticipated to reveal further involvement. Thus it is concluded that the family incidence of rheumatoid spondylitis lies between 9 and 13 per cent.

It was noted that among the relatives of spondylitics the incidence of extremity joint rheumatoid arthritis was less than 2 per cent. This was in marked contrast to the 9 to 13 per cent. incidence of spondylitis. It is suspected that the factors influencing the family incidence of rheumatoid disease are more closely related to comparable tissues in relatives than to connective tissue in general.

It is the responsibility of the managing physician to attempt to discover other cases of spondylitis among families of spondylitics.

Discussion

DR. ROBERT H. TALKOV (Boston, Massachusetts): A family survey of 293 cases of rheumatoid arthritis is being made (but is not yet completed) at the Massachusetts General Hospital for periods of ten to seventeen years, as compared with a control group of equivalent number and average figures of four series reported in the literature. The incidence of rheumatoid arthritis in one or more members of the family was 11·9, 5·3, and 20·6 per cent. respectively.

In a more detailed study 50 patients, selected in the order of their appearance at the clinic, were carefully questioned. Follow-up information was obtained by contacting or examining various members of the family, corresponding with their physicians, and searching hospital records. It was of interest to find that 32 per cent. gave a positive family history of rheumatoid arthritis, and in an additional 4 per cent. the occurrence of the disease was considered possible.

The records of 230 patients with rheumatoid spondylitis segregated into Group A (including shoulder and hip involvement) and Group B (including peripheral joint involvement) were studied. The familial incidence of rheumatoid spondylitis was 5·9 per cent. in Group A and 2·7 per cent. in Group B, whereas generalized rheumatoid arthritis was present in 1·2 per cent. of Group A and 8·9 per cent. of Group B. These figures appear to bear out those presented today, namely, that the incidence of spondylitis is greater in the families of those having spondylitis.

DR. HOWARD F. POLLEY (Rochester, Minnesota): Drs. Rogoff and Freyberg are to be complimented on the detailed manner in which this study was approached. One of the main difficulties in analysing a study such as this is brought out by their emphasis of the careful questioning that is necessary to elicit a complete and reliable family history. In our study of 1,035 cases of rheumatoid spondylitis reported last year at this meeting and to which Dr. Rogoff referred, several interesting features of the family history of patients with rheumatoid

spondylitis were noted. We examined two sets of identical male twins. In each instance one twin had rheumatoid spondylitis while in the other evidence of rheumatoid spondylitis or arthritis had not developed. The most extensive family history encountered was that obtained from a woman thirty-five years of age who had rheumatoid spondylitis. One of her brothers had died at the age of 42 after having had both rheumatoid spondylitis and peripheral rheumatoid arthritis for twenty years; another brother, aged 50 years, had had rheumatoid spondylitis and rheumatoid arthritis for eighteen years and a third brother, aged 38 years, had had rheumatoid spondylitis for seven years. The patient had three sisters who apparently did not have the disease.

In our series of 1,035 cases the recorded incidence of a family history of rheumatoid spondylitis was 0·4 per cent. the incidence of a family history of peripheral rheumatoid arthritis was essentially the same. The family history was not complete in all the cases in our series. We are, therefore, hesitant to emphasize these particular data without further study.

The finding of a family history of rheumatoid spondylitis or rheumatoid arthritis in cases of rheumatoid spondylitis is interesting, but other factors unknown at the present time may become more significant as understanding of the aetiology of rheumatoid spondylitis is advanced.

DR. R. M. STECHER (Cleveland, Ohio): These findings come as a great surprise to me because we investigated this subject and failed to find many references in the literature to the familial incidence of spondylitis. The disease does occur as multiple cases in the same family. Now that we have established the fact that it is a familial disease, the next step is to investigate the manner in which it is inherited, its genetic characteristics. For that, it is important that we know not only the number of people involved but also the number of people who are not involved, and it is also important to know how many members of the family there were, and I would suggest and hope that in all these studies, when they are finally published, they include not only the number of brothers but also the number of sisters.

Since our paper was published, we have been surprised at the additional cases that have come to our attention. We have had two sets of sisters. I have a letter from a man in Canada who had a set of brothers, and Dr. Kuhns has also given us a report of his figures.

DR. EDWARD F. ROSENBERG (Chicago, Illinois): I am sure this observation is sound and I have already put it to practical use. I am so convinced that the incidence of rheumatoid spondylitis is high among brothers of patients with this disease that I now urge radiographic examinations for all male siblings of spondylitis patients. By this means I discovered five cases in the past year.

DR. B. ROGOFF (closing): I am glad Dr. Rosenberg made that last comment. It is the responsibility of any doctor examining a case of rheumatoid spondylitis to question very carefully about relatives with any back disability, and it is his responsibility to examine those patients and institute proper treatment. Thus we may hope for better results.

Heberden's Nodes: Relationship of the Menopause to Degenerative Joint Disease of Fingers

ROBERT M. STECHER and
EDMUND E. BEARD

The time relationship of the development of Herberden's nodes to the menopause was observed in a hundred women. The exact onset of either event could not be sharply identified in most cases but, in general, it was found that Heberden's nodes occurred earlier in women with early menopause than in women with late menopause. The range of age of menopause was 28 to 56 years, the average age 48·55 years, the median age 49·3 years, and the standard deviation ± 5·2 years. These figures were similar to those found for a control group of 96 women. The age of onset of Heberden's nodes ranged from 33 to 65 years. The mean age was 48·8 years, the median age 48·8 years and the standard deviation ± 6·8 years. The coefficient of correlation for these two events in each individual was ± 0·459, ± 0·079, which is significant. These authors also discussed the possible influence of the known physiological changes of the menopause upon Heberden's nodes and other bone and joint disease, and the relationship of the menopause to other joint disease, to menopausal arthritis, and to menopausal arthralgia.

Discussion

DR. PHILIP S. HENCH (Rochester, Minnesota): Although Heberden's nodes are the most obvious expression of osteo-arthritis, little is known about them. Dr. Stecher and Dr. Beard suggest that the menopause may be casually related to the development of Heberden's nodes but they are *not* suggesting that Heberden's nodes constitute a form of " menopausal arthritis ". This distinction is important. Dr. Stecher and Dr. Beard derived little value from their review of the literature, which supports, with about equal fervour, four ideas: namely, that the menopause is definitely related to Heberden's nodes, that it is not, that it may be, or that nobody knows whether or not it is. In other words, previous workers have scarcely got beyond the realm of clinical supposition or speculation or the most elementary statistics. In support of the proposition of a relation between Heberden's nodes and the menopause, previous workers have offered no pathologic evidence indicating that the pathologic reactions in Heberden's nodes are of a distinctive type characteristic of " menopausal arthritis ", nor any impressive clinical evidence from the results of substitution or endocrine therapy.

Premature Heberden's nodes in women aged 30 to 35 years have been seen not uncommonly by Dr. Slocumb and myself. A sufficient number of these patients have also developed premature grey hairs or premature menopause or both to suggest to us the idea under discussion

and to make it seem attractive. However, these examples are rather striking exceptions, and in general we have been unable to link the menopause with the pathogenesis of Heberden's nodes.

I would draw the following six tentative conclusions: (1) The menopause is obviously *not* the *primary* aetiologic factor in Heberden's nodes. (2) The menopause may or may not be a secondary (conditioning or aggravating) factor in their development. (3) Despite statistics, the relationship between menopause and nodes may be largely coincidental, one no more definite than that between the menopause and the orderly development of grey hairs or mild arteriosclerosis or hypertension. (4) If the relationship between menopause and nodes is not purely coincidental it may be that the menopause is not the "parent" of the nodes but their "sibling" and that some other factor is the common cause of both menopause and nodes. (5) Since Heberden's nodes may develop among men, no unisexual hormone can be involved. If any hormone is concerned it must be bisexual, and one could hardly expect Heberden's nodes to respond to the use of female hormones. (6) When it is recalled that trophic disturbances of an extremity, such as those which occur with poliomyelitis in childhood, prevent forty years later the appearance of Heberden's nodes in the neurologically affected side, it is difficult to believe that a deficiency or an excess of any hormone can be the major cause of these nodes.

Until more hormone assays and other biochemical studies have been made in many cases of Heberden's nodes we cannot conclude that the menopause certainly constitutes an aetiologic factor of prime importance in the development of the osteo-arthritis of Heberden's nodes.

DR. RUSSELL L. CECIL (New York): At the time Dr. Archer and I published our study on menopausal arthritis, the criticism was made that these two conditions were purely coincidental and that what we were talking about was merely osteo-arthritis occurring in middle-aged women at the time of menopause. That was a fair criticism, but the fact remains that women who have artificial menopause, particularly in the twenties and early thirties, will often have severe arthralgia along with the other well-known signs of menopause. One would expect that if there were some connexion these pains would be relieved by oestrogen therapy. In my experience, however, the use of oestrogens in the treatment of these menopausal arthralgias has been disappointing.

Vitamin D Toxicity Simulating Hyperparathyroidism

CHARLES H. SLOCUMB

Vitamin D poisoning produced symptoms and also radiographic and laboratory findings similar to those of hyperparathyroidism, with or without changes in the bones, metastatic deposits of calcium, and renal damage which may or may not be reversible. The most common early symptoms of vitamin D toxicity were polyuria, polydipsia, nausea, vomiting, occipital headache, or pruritus. The early laboratory findings were elevated concentrations of serum calcium and blood urea and increased urinary excretion of calcium. Severe vitamin D poisoning produced deposits of calcium in nodules, tophi, and arteries, osteoporosis with destructive and cystic areas in bones, uraemia, and anaemia. Dosages of vitamin D as low as 50,000 units daily may produce severe toxic reactions. For no widely used preparation of vitamin D can the claim be made that it will not produce such toxic reactions. Recognition of vitamin D poisoning should temper such enthusiasm as remains for the therapeutic use of massive doses of this vitamin.

Discussion

DR. DAVID H. KLING (Los Angeles, California): In the arthritis clinic of the White Memorial Hospital and in private practice our experience was the same as Dr. Slocumb's.

(Several slides were demonstrated showing enormous metastatic calcification around the joints, which occurred in a 37-year-old patient with rheumatoid arthritis who took 150,000 to 250,000 units of vitamin D daily for about two years; a high alkaline ash diet with two quarts of milk daily was a contributing factor. By withdrawal of the vitamin D and change of diet, most of the metastatic calcifications disappeared in four months; the blood calcium dropped from 14 to 10 mg. per 100 c.cm. of blood. However, the shaft of the proximal phalanx of the fifth right toe showed a pathological fracture after the absorption of the calcification. The radiographs showed also arteriosclerosis of the popliteal artery, calcification in the kidney, and gallstones persisting after one year. The NPN remained high, over 60 mg. per cent., PSP excretion 25 per cent. Kidney damage therefore was irreversible.)

In a comparative study, 150 patients were treated with various brands of vitamin D for two to nine months; a dose of 100,000 to 250,000 units daily was given. Toxic reactions occurred in about the same percentage with the various brands, the therapeutic results being equally poor.

DR. RICHARD T. SMITH (Philadelphia): It is deplorable that there have been bushels of vitamin D passed out to patients all over the world, and so few cases of toxicity reported. We have had two cases of toxicity in Philadelphia, one in a 17-year-old boy with severe tophaceous gout, with a duration of three years, according to the history; because of the tophaceous gout in proximal interphalangeal joints, the diagnosis of rheumatoid arthritis was made. He was given vitamin D until he developed gastro-intestinal symptoms when it was temporarily stopped. The patient developed uraemia and died about two months after the vitamin D was again instituted. He had sheets of calcium in the soft tissues and in the tophi, which drained large amounts of calcium along with the urates. One of the draining tophi finally

spontaneously amputated through the terminal joint of a finger. There was no autopsy.

In another instance, a patient with spondylitis was given vitamin D and in a period of four months he showed symptoms of having renal calculi. Radiographs taken before the giving of the vitamin D showed no evidence of stones. When the symptoms began, there was radiographic evidence of stones and gravel in both kidneys.

Recently it has been called to my attention that a local physician going to a conference of supposed specialists in arthritis was told he should give vitamin D, one capsule a day, increasing even to nine a day, for arthritis. Vitamin D in concentrated forms is no longer a part of the programme of treatment at Jefferson. We have found evidence of calcium in the urine in patients who have taken only 50,000 units daily for seven days.

Nothing can be done to stop the practice of giving vitamin D as a prescription. The Pure Food Department would like it stopped but they cannot interfere as long as these preparations are sold on prescription. It must be up to us to stop the use of these dangerous drugs.

DR. PHILIP S. HENCH (Rochester, Minnesota): Vitamin D toxicity can be serious. As Dr. Slocumb has demonstrated, it can simulate hyperparathyroidsm or can produce other clinical pictures, with the development of mental confusion or even (non-uraemic) coma, or chronic nephritis with transient uraemia or with persistent progressive fatal uraemia. Much of the commercial advertising of concentrated vitamin D preparations for arthritis has been blatant, false, and objectionable, revealing half-truths and concealing or failing to mention the chances of significant toxicity. However, the advertising has been so effective that nowadays concentrated vitamin D is being given, not only for rheumatoid arthritis, but a for variety of arthritides such as osteoarthritis or gout, or even for " aches and pains ". Thus one must be on the alert to recognize vitamin D intoxication in anyone with " rheumatism ", not only in those with rheumatoid arthritis.

Our metabolic experts at the Mayo Clinic have become aware of the current dangers of making a diagnosis of hyperparathyroidism (on previously acceptable grounds) in a rheumatoid or " rheumatic " patient, and in all such cases they now question the patients carefully relative to the use of any preparation of vitamins. However, often the patient is unaware that he has taken concentrated vitamin D. Some time ago I saw a patient with " muscular rheumatism " who was scheduled for parathyroidectomy the next day because, though she was sure she had taken nothing but two varieties of salicylates, she presented biochemical features of hyperparathyroidism and had diffuse musculoskeletal pains. We telegraphed to her physician and learned that when the first medication (salicylates) had given inadequate relief he had substituted concentrated vitamin D, which the patient thought was just another salicylate. The case turned out to be one of vitamin D toxicity involving a myofibrositic patient.

Even more instructive and disturbing was the following case. An arthritic patient presented enough features of " coincidental hyperparathyroidism " to be listed for parathyroidectomy. At operation the surgeon could not find any tumour. Somewhat embarrassed, he turned to the gallery and assured them that he and the clinicians, having been quite aware of the possibility of vitamin D toxicity in an arthritic patient, had been informed emphatically by both the patient and the attending home physician that no vitamins had been given. At this juncture a voice from the gallery meekly said, " I wonder if the medicine I've been giving the patient is responsible." To this the suprised surgeon replied, " But what do you know about this case? Are you her home physician? " " No," answered the visiting physician, " I'm a relative and have been giving her vitamin D on the side." Thus it appears that sometimes not even the responsible attending physician knows that vitamin D preparations are being taken—truly a dangerous situation.

Because nephritis is so rare in cases of rheumatoid arthritis, I have used a maxim which was valid for many years: In a case of acute, recurring or chronic arthritis with nephritis or renal stones, suspect gout. However, rheumatologists are now encountering two varieties of of " pharmaceutic nephritis ", that from gold and that from concentrated vitamin D. Hence we must modify the maxim and restate it thus: In a case of acute recurrent arthritis with nephritis or stones (radiographically non-opaque), think of gout, but in a case of chronic arthritis or even of vague " rheumatism " with nephritis or stones (radiographically visible) think of rheumatoid arthritis with pharmaceutic nephritis, chiefly vitamin D intoxication, and less commonly " gold nephritis ".

DR. WALTER BAUER (Boston, Massachusetts): I am not surprised to learn of Dr. Slocumb's observations. On the basis of our own experience, I feel certain that such toxic reactions occur much more frequently than the medical literature indicates. In fact, intoxication may result from much smaller doses of vitamin D than those usually employed in the treatment of rheumatoid arthritis. We have observed a hypercalcaemia varying from 11·2 to 14·2 mg. per 100 c.cm. of blood for a period of twenty-five weeks, during which time the daily dose of vitamin D never exceeded 60,000 U.S.P. units.

Dr. Slocumb's report calls to our attention many interesting features of vitamin D poisoning. As he points out, the renal lesions may be severe and long-standing. It is important to remember that in some instances they have been irreversible. In view of this latter fact, one might postulate that some of his cases may have developed secondary hyperparathyroidism of the type occasionally seen in association with chronic nephritis. Review of his data with this point in mind may throw additional light on the nature of the biochemical changes he has observed.

DR. CHARLES H. SLOCUMB (closing): Renal stones were not mentioned because only two of the patients had renal stones. My associates and I were unable to demonstrate that these patients had not had the stones before they took vitamin D. However, the stones may have been related to the vitamin D poisoning.

I did not mean to imply that vitamin D poisoning

produced arteriosclerosis, but it does cause deposits of calcium in the media of arteries. This has been well established in the pathologic studies of persons who have died of vitamin D poisoning. The deposits of calcium in the arteries may be distributed so finely that they may not show in radiographs.

I cannot answer the question regarding secondary hyperparathyroidism other than to point out that in the cases of renal damage that we have followed for two and a half to three years the concentration of calcium in the serum returned to normal, and that of phosphorus remained slightly elevated or returned to normal even though the concentration of urea did not go below 64 to 92 mg. per 100 c.cm. of blood. In spite of the renal damage these patients regained good health.

Rheumatoid Arthritis in Patients Receiving Simple Medical and Orthopaedic Measures

CHARLES L. SHORT and WALTER BAUER

This report is based on a follow-up study of 250 unselected patients with rheumatoid arthritis admitted to the medical wards of the Massachusetts General Hospital between 1930 and 1936. No patient was included who had received gold or vitamin D in massive dosage, whose follow-up was inadequate, or in whom the diagnosis was in question. The patients were rarely kept in the hospital more than a few weeks for diagnosis and accumulation of data and to receive instruction in general measures which could be carried on at home. Fifty-six patients died in the course of the study, with the results in such cases expressed according to the latest examination before death.

The average duration of follow-up was 9·6 years, with 80 per cent. under observation for more than five years. The latest examination of these patients gives the following results: improved, 53 per cent.; stationary, 13 per cent.; and worse, 34 per cent. Of the improved group, thirty-eight, or 15 per cent. of the series, were in remission. The most striking factor affecting prognosis was found to be the duration of the disease. Nearly three-quarters of those with duration of one year or less showed some degree of improvement, with an even higher percentage in patients seen in the first six months. In addition, males without spondylitis, patients under 40, those with asymmetrical joint involvement, and those with mild involvement, activity, and total severity were likely to have a more favourable outcome. Factors of no importance in determining the patients' course included involvement of the spine, a history of prodromal symptoms, an intermittent course before admission, and an acute contrasted with a gradual onset. Others were a severe degree of anaemia, a family history of rheumatoid arthritis or rheumatic fever and, in women, onset within two years of the menopause.

The net relapse figures (35 per cent.) are comparable to those tabulated from a combined series of 768 patients improving under gold therapy. Twenty-three patients, or 9·2 per cent., could be considered " five-year cures ".

In summary, certain clinical factors of prognostic value in rheumatoid arthritis have been outlined. But we have chiefly attempted to present a control series which may be used for comparison with groups of patients receiving special forms of therapy.

Discussion

DR. OTTO STEINBROCKER (New York): I admire the courage and persistence of the authors in carrying such a large group of patients for so long a period on ordinary measures. It must have been difficult to follow this course in spite of the many therapeutic enthusiasms of the past ten years, which must have been tempting.

There is no control group of patients in the literature, to my knowledge, carried for a long period without treatment, permitting us to study the uninfluenced evolution of the disease. This series approaches closest to that. This paper therefore constitutes, in my opinion, one of the fundamental contributions to therapeutic investigation of rheumatoid arthritis. It gives some of the essential facts of life in rheumatoid disease, by means of an extensive follow-up of the response to general measures and/or the lapse of time. Such basic information had been sorely needed in our understanding of the disease.

The control studies available are all too few and they usually lack lengthy follow-up. This paper provides for comparison two types of information to be distinguished in any special therapy. Initial response to treatment after an arbitrary period or course; and long-range results, which are much more important. It gives a therapeutic base line, at least for significant response, above which results of any palliative or specific must rise appreciably under the same conditions. It should prove a real asset for comparison of results for those clinics or individuals whose material is too limited to permit a control series of their own.

The response of different stages of rheumatoid arthritis may be a factor in the results. It would be helpful if, in the final report, such a classification is included together with the response of each stage.

DR. RICHARD H. FREYBERG (New York): This paper should become a basis for evaluation of special measures of therapy. However, there are certain factors not mentioned by the authors which should be taken into consideration. One is the speed with which improvement may occur, to bring about remission in the disease. This is important to the patient; any special measure of treatment which will lessen disability, leaving more hours and days of comfort and ability to work, has very significant value. This should be taken into consideration.

A second factor is that of control by comparing different periods in the course of illness in the same patient, one period when no special therapy is used and another when a certain special measure is employed. This form of control becomes exceedingly difficult for, as Dr. Short has pointed out, what happens during one year in the course of this illness may in nowise be an index as to what may happen in another year in the same patient. Many times, however, this form of control is of distinct value, and it has not been used in this analysis.

DR. CHARLES L. SHORT (closing): We had in mind the creation of a series something like this from the beginning, and we purposely refrained from giving the patients, or at least very many of them, so-called specific treatment. These were patients who came into the hospital, it is true, and possibly other series could be set up with patients of milder severity who came to a clinic. On the other hand, they do represent a cross-section, because certainly the minority of them were classified as severe.

We are not claiming that this form of treatment—that is, simple, general measures—necessarily has an effect on the course of the disease. I think that it is an open question, and Father Time must be given his due share of the credit.

As to the point Dr. Freyberg made about speed of improvement, I will say briefly that of the patients that showed ultimate improvement, in about two-thirds of them that improvement was manifest in two years, and in nearly four-fifths, within four years. We can also see from this series that a remission is possible and may occur even after the patient has been under observation a number of years.

La Session annuelle de l'American Rheumatism Association

Un symposium sur le collagène s'est tenu à New Jersey, le 7 juin 1947. La structure microscopique du collagène a fait l'objet de recherches au Massachusetts Institute of Technology pendant les cinq dernières années, et le Dr. J. Gross a déclaré qu'il pensait que la découverte de la structure du collagène et des substances voisines pouvait fournir une base pour une meilleure compréhension de quelques troubles pathologiques qui se produisent dans les tissus conjonctifs. Le Dr. K. Meyer déclara que, histologiquement, il existe deux types se substances interfibrillaires: la substance fondamentale amorphe et visqueuse; et les céments métachromatiques proprements dits. Tous deux sont constitués principalement par des protéines et des polysaccharides. On peut faire entrer en corrélation la chimie des tissus conjonctifs et leur histologie en admettant que le substance fondamentale amorphe contient de l'acide hyaluronique tandis que les céments contiennent différents sulfates de chondroïtine comme constituants principaux.

Le Dr. C. V. Z. Hawn cita des expériences faites sur des lapins dans le but d'établir la corrélation entre la série des modifications pathologiques et immunologiques, et de comparer les réponses aux deux fractions chimiquement et immunologiquement distinctes des protéines plasmatiques et au sérum entier de la même espèce. Le Dr. P. Klemperer conclut qu'il est nécessaire d'acquérir des connaissances plus fondamentales sur la nature et la cause de l'altération fibrinoïde des fibres de collagène avant de pouvoir attaquer le problème de l'étiologie de la maladie humaine caractérisée par les modifications du collagène diffus.

D'autres communications portaient sur les rhumatisants dans les forces armées (May G. Wilson et ses collaborateurs), les modifications cardiaques dans l'arthrite rhumatismale (W. S. Clark et W. Bauer), le caractère familial de la spondylite ankylosante (B. Rogoff et R. H. Freyberg), les nodules d'Heberden, et les rapports entre la ménopause et la maladie dégénérative des articulations des doigts (R. M. Stecher et E. E. Beard), la toxicité de la vitamine D simulant l'hyperparathyroïdie (C. H. Slocumb), et l'arthrite rhumatismale chez les malades recevant de simples traitements médicaux et orthopédiques (C. L. Short et W. Bauer).

ABSTRACTS

[This section of the ANNALS *is published in collaboration with the two abstracting Journals,* Abstracts of World Medicine, *and* Abstracts of World Surgery, Obstetrics and Gynaecology, *published by the British Medical Association. The abstracts are divided into the following sections: acute rheumatism; articular rheumatism (rheumatoid arthritis, osteo-arthritis, spondylitis, miscellaneous); gout; non-articular rheumatism; general articles. After each subsection of abstracts follows a list of articles that have been noted but not abstracted. Not all sections may be represented in any one issue.]*

Acute Rheumatism

Some Public Health Aspects of Rheumatic Fever. WHEATLEY, G. M. (1947). *W. Va. med. J.*, **43**, 57.

The last ten years have been important in the control of rheumatic fever, chiefly because: (1) the war has helped greatly in understanding its epidemiology; (2) more doctors have become aware of the need to apply this knowledge; (3) (in America) the American Rheumatic Fever Council has been a spearhead in the attack.

The success or failure of control efforts must be judged partly by recurrence rates, and Wilson and Lubschez (*J. Amer. med. Ass.*, 1944, **126**, 477) found that the chance of a major recurrence was two to three times as great in the year following the attack as in one, two, or more years after; also that age was important in assessing the likelihood of a recurrence (25% chance with children aged 4 to 13, 8·6% when aged 14 to 16, and only 4% when aged 17 to 25). Family susceptibility plays a part; but why must a child reach school age before he acquires the disease in recognizable form, and why does not the child of school age bring it back to the pre-school child at home? Other factors are geographical and seasonal variation; in three areas of America the incidence is very high (Rocky Mountain states, Great Lakes region, and middle Atlantic states), in southern California and the middle west very low. There is also the seasonal variation, highest incidence in April, lowest in November. Also must be mentioned the steady decline in mortality from rheumatic fever and rheumatic heart disease in children since 1910.

No way is known of preventing the initial attack. Methods tried in the past to prevent recurrences include transfer to a warmer climate, improving the diet, removal of tonsils, and the prophylactic use of drugs such as salicylates and sulphonamides. None of these has a specific effect. With sulphonamide prophylaxis, out of six groups the recurrence rate in those treated was only 2·3% with no deaths, in the controls 22·6% with six deaths. But there is the danger of producing sulphonamide-resistant strains of the streptococcus. Salicylate therapy has not been convincing, and tonsillectomy should be carried out only for normal reasons. Methods of dust control by penicillin, ultra-violet light, etc., have also been tried.

The complex nature of the disease produces certain problems which cannot be solved by the practising physician alone; he needs to be able to make use of a consultant when necessary, and also to be able to recommend his worst crippled patients for occupational therapy. Convalescence is often prolonged and expensive, and the community should play a part in easing the financial burden. In the U.S.A. a start has been made, since 1939, by the Children's Bureau, and since February, 1944, by the Council on Rheumatic Fever of the American Heart Association. In one State and a few of the largest cities campaigns have been started to educate people in the subject of rheumatic fever; but it is admitted that none of the schemes are as well co-ordinated as the London County Council's scheme of 1927, although some of the cities (for example, Syracuse, N.Y.) have based their programmes on the ideas of the L.C.C. Statistics since 1927 show that all the money and hard work spent on the scheme have been worth while; for whereas 2% of the school children of London in 1926 suffered from acquired heart disease, the figure had fallen by 1936 to 0·8%. *T. G. C. Early.*

Rheumatic Heart Disease in the Adult. EGGLESTON, C. (1947). *Amer. J. Med.*, **2**, 278.

The author is not convinced of the relationship between haemolytic streptococcal infection of the upper respiratory tract and the reactivation of the rheumatic process in the susceptible individual, nor of the value of sulphonamide prophylaxis. The clinical manifestations of the disease are more important than laboratory tests both in diagnosis and in deciding when active rheumatic disease has ceased. In the active phase adequate care will minimize cardiac damage, which in the polycyclic type may affect the heart muscle more than the valves. A positive throat culture does not necessarily signify rheumatic activity.

Rheumatic heart disease in the adult may be classified into four categories: (1) active rheumatic fever with evidence of carditis, endocarditis, or pericarditis; (2) cases showing physical signs of valvular disease but no evidence of present activity; (3) active rheumatic fever with residual valvular disease; (4) bacterial endocarditis. Active rheumatic carditis is probably as common in the adult as in the child, and the author maintains that serial sections of the heart from autopsies on the rheumatic adult would show histological evidence of rheumatic activity in a great majority of cases. Mitral stenosis is of no prognostic value except that a first appearance in adult life is less serious than a childhood affection. Auricular fibrillation may be transient or permanent, and, if congestive heart failure supervenes, control is more readily affected when auricular fibrillation is present than when the pulse is regular. Rheumatic pericarditis is not of such serious prognostic significance as it was formerly

considered to be. The diagnosis of early bacterial endocarditis may be difficult, and recurring pulmonary infarction is a clinical manifestation not ordinarily emphasized. There is no advantage in giving salicylates intravenously rather than orally. Convalescence should not be hastened, and later the general physical health should be maintained as high as possible while patients should be allowed to be as active as they are able. If pregnancy occurs, it should be interrupted only if there is evidence of heart failure, and labour should be made as easy as possible. Active rheumatic carditis is a valid reason for terminating pregnancy. *T. G. Reah.*

The Electrocardiogram in the Diagnosis and Management of Rheumatic Fever. SOKOLOW, M. (1947). *Calif. Med.*, **66**, 221.

The diagnosis of rheumatic fever in adults is sometimes difficult, particularly where there is no previous history, no cardiac enlargement, and no diastolic murmurs. In some instances the electrocardiograph may reveal significant changes. In a series of 700 cases reported in this paper, electrocardiographic abnormalities were found in 144, the most important being A-V block in 86 and T-wave changes in 52. The diagnosis of A-V block was made when P-R interval was over 0·20 seconds or if with clinical improvement a decrease in at least 0·04 seconds occurred. These changes may be surprisingly transient and intermittent, and the frequency of abnormal tracings depends on the frequency with which E.C.G.s are taken. T-wave changes are best shown by serial records, progressive changes towards normal through diphasic, flat, and low T-wave stages being found. Lead 4 may be the only one to show changes.

In addition to being valuable in diagnosis, electrocardiography is useful in following the course of rheumatic fever, particularly in the polycylic forms, many of which are sub-clinical; in such cases the reappearance of abnormalities in the E.C.G. may be the only objective sign of recrudescence. *H. A. Burt.*

The Action of Salicylates in Rheumatic Fever. GLAZEBROOK, A. J., and COOKSON, B. (1947). *Edinb. med. J.*, **54**, 193.

The authors describe Maclagan's first use of salicin in the treatment of acute rheumatism and point out that he recognized that it was not likely to benefit the carditis. They describe a series of 103 patients suffering from rheumatic fever who had been treated with anti-streptococcal serum or with human convalescent serum and not with salicylate, in which the incidence of carditis was no higher than in comparable groups treated with salicylate.

They recall Coburn's claim that a plasma salicylate concentration of 36 mg. per cent. would prevent carditis, and that to maintain this level intravenous administration of salicylate was indicated. But other workers had not been able to confirm these claims. Taran and Jacobs, while unable to agree with him on the prevention of carditis, agreed that his high plasma salicylate was desirable, and in 18 children whom they treated with salicylate by mouth found toxic symptoms manifested as tachypnoea in only 1. Other workers found a varying incidence of toxic symptoms, the incidence of which was always higher in patients to whom the drug was given intravenously, and " opinions seem to be hardening against the intravenous method of treatment ". Sufficiently high plasma salicylate concentrations can be obtained by oral administration.

The authors discuss the role of bicarbonate, which is traditionally given with salicylate. Some say that it prevents a fall in alkali reserve, others that the salicyl radical specifically stimulates the respiratory centre and, by causing a loss of carbon dioxide by hyperpnoea, raises the alkali level of the blood which causes the excretion of alkaline urine and therapy a secondary loss of fixed alkali. These authors suggest that both these mechanisms may play their part, and agree with others that bicarbonate alleviates the dyspnoea of salicylism by depressing the blood salicylate level; while a daily dose of 8 g. of sodium salicylate will achieve a plasma salicylate level of 36 mg. per cent. in an adult, 12 g. of salicylate will be needed to achieve this level if it is given with an equal dose of bicarbonate. They suggest that salicylate should initially be given without bicarbonate, and that the latter should be given later if symptoms of salicylism occur. They note the work of Dry, Butt, and Scheifley, which showed that para-amino benzoic acid if given with salicylate and bicarbonate raises the blood salicylate level.

The possibility that salicylate may lower the blood prothrombin level and exert an anti-coagulant effect has been the subject of conflicting reports. There is evidence that a pre-existing ascorbic acid deficiency may predispose to a fall in prothrombin index when salicylate is administered. In a controlled series of patients suffering from rheumatic fever and treated with salicylate and bicarbonate, the authors found that while the administration of salicylate did cause a fall in prothrombin level in both rheumatic and non-rheumatic subjects, it was moderate only. Vitamin K raised the prothrombin index of salicylate-treated normals in all but one of series of 7. The authors note that while much work on this subject was stimulated by Link's suggestion that dicoumarin was degraded by the body into salicylate, this suggestion is not securely founded.

All 20 patients in their series noticed symptoms of salicylism, and 2 were so severely affected that administration of the drug had to be stopped. In the rest the salicylate discomfort was greater initially and rapidly improved.

It may be that salicylate antagonizes a product such as pantothenate which is known to be produced by certain bacteria. Recently Guerra has shown that in rheumatic conditions the hyaluronic acid of the connective tissue is damaged by a hyaluronidase, and suggests that salicylate acts by inhibiting this enzyme. Coburn and Kapp suggest that salicylate inhibits the antigen-antibody reaction which they claim to be disordered in rheumatic fever. The authors speculate on the possibility that the effect of salicylate is to prevent the internal clotting of cells brought about by an antigen-antibody reaction which may have an irritant effect. They recall experiments which have demonstrated the anti-anaphylactic properties of heparin, and do not think that " its appearance in the blood during anaphylactic shock can be dismissed as an unimportant side effect ". There is experimental evidence that histamine or a substance like it may be produced by anaphylactically reacting cells and that this production of histamine can be inhibited by adequate amounts of heparin. They speculate further on the relationship between the highly accelerated ascorbic acid utilization in rheumatic fever and the possible part played by ascorbic acid in tissue respiration. Finally they suggest a correlation between the known beneficial effect of jaundice in severe chronic rheumatism and the reduction in the coagulability of the blood known to occur when bile is present in the blood stream.

W. Tegner.

Prophylactic Sulphanilamide in Rheumatic Fever: Preliminary Report. STOKES, H. L. (1947). *Proc. R. Aust. Coll. Phys.*, **2**, 16.

The author presents the results to date of sulphanilamide prophylaxis in convalescent and quiescent cases of rheumatic fever. His experience extends over 2 years, during which time sulphanilamide was given to 238 children in doses ranging from 0·5 g. per day to 0·5 g. three times a day. Toxicity was not found to be a serious limiting factor. Close co-operation was maintained with the bacteriological department, and throat swabs and typing were studied in a high proportion of cases. There was no significant decrease in carrier rates of haemolytic streptococci in the treated as opposed to the control group, although there appeared to be a decrease in the number of clinical relapses in the control group. Furthermore the percentage of organisms resistant to sulphanilamide rose significantly in the treated series, from 7·1 to 31%.

The author comments on these interesting findings, and refers to the experience of American workers in the same field, who found that the induction of drug resistance was a definite danger. It is suggested that prophylactic use of sulphanilamide may be unwarranted, or even dangerous, though as yet there is no proof that the drug-resistant organisms isolated were in fact of the same type as those found in throat swabs before drug therapy.

[The author is continuing this survey; further figures and bacteriology should prove of value.]

David P. Nicholson.

Penicillin Prophylaxis in Acute Rheumatism. BURKE, P. J. (1947). *Lancet*, **1**, 255.

Penicillin by mouth is suggested as an alternative to sulphonamides in the prophylaxis of acute rheumatism. [No reference is made to any clinical observations for nicotinamide deficiency in the treated patients.]

T. G. Reah.

The Differential Diagnosis of Adult Rheumatic Fever and Rheumatoid Arthritis. ENGLEMAN, E. P. (1947). *Calif. Med.*, **66**, 277.

The differential diagnosis of acute rheumatoid arthritis occurring in young adult males and adult rheumatic fever occurring without a previous history of acute rheumatism and without signs of cardiac involvement may be exceedingly difficult. In this paper "the most helpful differential diagnostic features" are outlined, the most significant being (1) the presence or absence of residual changes in the joint, and (2) the response to salicylates. In rheumatic fever residual changes almost never occur, whereas in rheumatoid arthritis they are the rule. Salicylates have little effect with rheumatoid arthritis; in rheumatic fever objective signs such as effusion invariably clear up with salicylates, though they may take 18 days to do so. It is emphasized that rheumatic fever patients frequently continue to experience joint pain for several months in spite of adequate salicylates though physical signs in the joints themselves are absent.

H. A. Burt.

Laboratory and Clinical Criteria of Rheumatic Carditis in Children. TARAN, L. M. (1947). *N. Y. St. J. Med.*, **47**, 703.

Some Observations on the Prevalence of Rheumatic Heart Disease in Canada. KEITH, J. D., and PEQUEGNAT, L. A. (1947). *Can. J. publ. Hlth.*, **38**, 111.

Acute Abdominal Appearances in Rheumatic Fever. (Cuadros agudos de vientre en la fiebre reumatica.) PIAGGIO BLANCO, R. A., DUBOURDIEU, J., and CASAMAYOU, E. (1947). *Rev. argent. Reumatol.*, **12**, 4.

Rheumatic Brain Disease: Late Sequel of Rheumatic Fever. BRUETSCH, W. L. (1947). *J. Amer. med. Ass.*, **134**, 450.

Rheumatic Fever. (A rheumés lázrói.) KELEMEN, E. (1947). *Orvostud. Beszám.*, **1**, 475.

Articular Rheumatism

(Rheumatoid Arthritis)

Studies of the Peripheral Circulation in Rheumatoid Arthritis. [In English.] ROUTTI, O. (1947). *Ann. Med. intern. fenn.*, **36**, 158.

The author reviews the literature on the peripheral circulation in rheumatoid arthritis and concludes that circulatory disturbances are not now regarded as an aetiological factor. He describes his air plethysmograph and the methods he used to study the circulation in the forearms and hands of patients suffering from rheumatoid arthritis and of controls. He found wide variation in the circulation of normal controls, for "the maximum circulation of the healthy test subjects was in fact 5 times greater than the minimum". In rheumatoid arthritis when there was no active inflammation the circulation was similar to that of normals. This was surprising in view of the fact that there is agreement that capillary microscopy reveals a diminution in the peripheral circulation of such patients. Where there was inflammation of the hands the circulation was increased above that of normals.

The author discusses his methods and possible criticisms of his technique. He concludes that his findings, although apparently not in agreement with the finding by capillary microscopy that the circulation in the nail bed is retarded, may mean that while circulation in the nail bed and skin is slowed down, in the limb as a whole it is unaffected.

W. S. Tegner.

Investigations of the Cerebrospinal Fluid in Cases of Rheumatoid Arthritis. SUNDELIN, F. (1947). *Amer. J. Med.*, **2**, 579.

The author points out that the symptomatology of rheumatoid arthritis includes a number of neurological symptoms which indicate involvement of the central and autonomic nervous system. Such symptoms include: (1) muscle atrophy, (2) paresis, (3) tremor of the fingers and hands, (4) trophic (autonomic) disturbances.

The author studied 141 cases (38 male, 103 female); 58 (41%) had spinal-fluid protein values (Izikowitz method) which were pathological in one way or another, and a total of 66 (46·8%) had fluids which were in some way changed pathologically. The mean value of the total protein of the spinal fluid in normal women was taken as 31 mg. per 100 ml., and the maximum "permissible" statistically calculated normal value as 48·7 mg. per 100 ml.

The protein was above normal limits in 6 cases, all in women, the values varying between 51 and 67 mg. per 100 ml. The globulin content exceeded normal limits in 17 cases, the normal mean value being accepted as 7·7 mg. per 100 ml. and the maximum " permissible " value as 13·7 mg. per 100 ml. for men, with values of 6 and 10·7 mg. per 100 ml. for women. The values for men varied between 14 and 21 mg. per 100 ml., and for women between 11 and 28 mg. per 100 ml. The albumin content was increased in 6 cases, all in women, and varied between 38·9 and 46·2 mg. per 100 ml. (normal mean value 22·9, and maximum " permissible " value 38·4 mg. per 100 ml.). The globulin–albumin quotient was abnormally high in 52 cases (14 men, 38 women). The author states that if a comparison is made between the total protein values obtained and the normal values found in large series no considerable difference appears, but the globulin-albumin ratio is considerably altered, the mean value being 0·36 as compared with a normal value of 0·25.

As the colloidal gold reaction is conditioned by the J-globulin, the gold-sol reaction was investigated in 107 cases; 15 reactions were pathological. Neither the degree of severity of the disease nor the duration of illness appeared to affect the protein values. Seven cases had an increased spinal-fluid cell count. All the patients with a pathologically increased protein content, except 1, exhibited one or more neurological symptoms.

S. Oram.

Serum Lysolecithin in Rheumatoid Arthritis, Pregnancy, and Jaundice and in Normal Persons. KUZELL, W. C., and DAVISON, R. A. (1946). *J. Lab. clin. Med.*, **31**, 1223.

An investigation was undertaken to discover whether the remissions in rheumatoid arthritis which are known to accompany pregnancy and jaundice were associated with any change in the serum lysolecithin level. It was found that the mean values were the same in normal controls, rheumatoid arthritis, pregnancy, and jaundice. No relationship between the lysolecithin values and the erythrocyte sedimentation rate could be demonstrated.

R. Bodley Scott.

Rheumatoid Arthritis: V. The Agglutination of Hemolytic Streptococci. WALLIS, A. D. (1947). *Amer. J. med. Sci.*, **213**, 94.

Relatively feeble agglutinins for the group A streptococcus have been found to occur in the sera of normal individuals. The author thinks the increased ability of the sera of patients with typical rheumatoid arthritis to agglutinate selected strains of group A streptococcus is due to the non-specific enhancement of these antibodies. This property of the serum is apparently related to the ability to agglutinate suspensions of fine collodion particles.

T. D. M. Martin.

Prolonged Administration of Sulfonamides in Rheumatoid Arthritis. [In English.] VIRKKUNEN, M. (1947). *Ann. Med. intern. fenn.*, **36**, 198.

Rheumatoid arthritis was treated in 38 cases with various sulphonamide drugs for long periods. There was improvement in all but 6 cases. Sensitivity reactions caused by the sulphonamides produced a sharp and definite therapeutic effect. After treatment was stopped 15 cases were studied for 2 months, and the condition of only 3 remained good.

A. Kekwick.

Blood Transfusion in the Treatment of Rheumatoid Arthritis. APPLEQVIST, O., and HOLSTI, Ö. (1947). *Schweitz. med. Wschr.*, **37**, 977.

Twenty-four mostly severe cases of rheumatoid arthritis, 15 women and 9 men, were treated with from 2 to 13 weekly blood transfusions in addition to " a certain basic treatment ". The impression was in most cases favourable and confirmed scanty earlier experience although dramatic improvements were rare. The authors think that blood transfusion might well be given (in preference to and before resorting to gold therapy) a fair trial in the form of a long series. They suggest that the most suitable patients would be young and anaemic ones in an early stage of the disease. Further studies are being made.

From the Author's summary.

On the Occurrence of Keratoconjunctivitis Sicca in Cases of Rheumatoid Arthritis. [In English.] STENSTAM, T. (1947). *Acta med. Scand.*, **127**, 130.

The earlier work of Sjögren the syndrome of keratoconjunctivitis sicca with arthritis is referred to. The symptoms are smarting pain and a gritty feeling in the eyes, and reduced tear secretion. The conjunctiva stains strongly with bengal rose. Dryness of the nose and pharynx may occur, and 80% of patients also suffer from chronic arthritis. Sjögren regarded the syndrome as a distinct disease.

The author draws his material largely from the rheumatological clinic at Lund Hospital, Sweden. He finds that 10·5% of cases of chronic rheumatoid arthritis have typical keratoconjunctivitis sicca.

H. F. Turner.

Arthritis Mutilans [In English]. NIELSEN, B., and SNORRASON, E. (1946). *Acta radiol., Stock.*, **27**, 607.

Three cases of arthritis mutilans in patients with long-standing polyarthritis are reported. In all, the destructive process was confined to the metacarpophalangeal and proximal interphalangeal joints; there were no destructive changes in the distal interphalangeal joints. This disease is found predominantly in females. Its onset is apparently insidious, though no patients have been followed up and radiographed over a long enough period to be certain of this. Apart from the destructive changes localized to certain joints, there appears to be no feature to distinguish the condition from ordinary polyarthritis. Histologically, fatty degeneration is sometimes seen in the bones. This is not found in chronic polyarthritis, but the author considers that it is probably a secondary change due to disuse resulting from the increased degree of immobility following on the destructive changes. Vascular changes are minimal and there is no evidence of nerve degeneration. It is considered that arthritis mutilans (*main en lorgnette* syndrome) exists as a separate entity, but that there is no sharp dividing-line between mutilating and non-mutilating varieties of chronic polyarthritis.

P. Kerley.

Contribution to the Study of Variations in Fibrinogen Levels in Progressive Chronic Polyarthritis. (Contribution a l'étude des variations du taux fibrinogène dans la polyarthrite chronique évolutive.) COLINET, E. (1947). *Arch. Rheum.*, 7, 72.

The fibrinogen content of the plasma in cases of chronic progressive polyarthritis is determined, and a relation established between fibrinogen level and erythrocyte sedimentation rate. If the fibrinogen values are plotted as abscissae and the corresponding erythrocyte

sedimentation rates as ordinates, a curve results with the form of a hyperbola. The fibrinogen value, that is, rises more slowly with increase in the E.S.R. It reaches a maximum value of about 6 mg. per ml. of plasma; this corresponds to an E.S.R. of 60 to 70 mm. in 2 hours by the Westergren method. The value does not increase further with increase in the E.S.R. With clinical improvement the fibrinogen value returns very slowly towards the normal, but it is rare to find complete return to a normal figure. *Kenneth Stone.*

Disturbance of Glucose Metabolism in Progressive Chronic Polyarthritis. (Troubles du métabolisme glucidique au cours de la polyarthrite chronique évolutive.) POLONOVSKI, M., COSTE, F., and DELBARRE F. (1947). *Bull. Soc. méd. Hôp. Paris*, **63**, 489.

Glucose-tolerance tests were performed on 16 patients suffering from progressive chronic polyarthritis; 50 g. glucose was given by mouth and the blood sugar observed for 3 hours subsequently. The authors conclude that in this condition there is a disturbance of glucose metabolism for which there is no explanation.

T. G. Reah.

Penicillin in the Treatment of Keratosis Blennorrhagica with Polyarthritis. FREIREICH, A. W., SCHWARTZ, S., and STEINBROCKER, O. (1947). *Arch. intern. Med.*, **79**, 239.

Keratosis blennorrhagica with polyarthritis is a rare condition occurring about once in every 5,000 cases of gonorrhoea. The symptoms are urethritis, arthritis, and dermatosis. Chills and fever accompany the malady, which follows chronic or relapsing gonorrhoea. The urethritis is typical of a chronic insufficiently treated gonorrhoeal infection. The arthritis is usually widespread, variable, and polyarticular, and the lesions of the skin consist of vesicles, pustules, and crusts with widespread thickening and desquamation of the skin. The crusts may pile up under the nails and separate them from their beds. Diffuse osteoporosis can sometimes be detected, especially in the wrists; and occasionally proliferative change in the periosteum of the manubriosternal articulation. The present series consists of three cases, two of which were cured with penicillin; the third patient came too late for treatment and died.

G. F. Walker.

Three Cases of the Felty Syndrome. [In English.] YTREHUS, O. (1947). *Acta med. Scand.*, **126**, 437.

The syndrome described by Felty in 1924 (of chronic polyarthritis, splenomegaly, and leucopenia) appears to have evoked little comment in the English literature, though a number of cases have been reported from Europe, Scandinavia, and America. Ytrehus reports three further cases in women aged 38, 57, and 60 years with polyarthritis of 13 to 19 years' duration who on repeated examination showed splenomegaly and leucopenia, with granulopenia and preponderance of young forms. One patient died, apparently of generalized sepsis, but autopsy revealed no distinctive pathological or histological features.

Splenectomy was not performed in any of these cases, though one patient had a sister who had been treated by splenectomy for the same syndrome (result not stated). Several surgeons have reported good results on marrow function and articular symptoms following removal of the spleen in cases of the Felty syndrome, and this would seem to be a justification for its recognition. However, the results as published were not invariably as strikingly good, and there is, so far, no reason to ascribe the syndrome to any definite causative agent. The granulocytopenia may be due to an alteration in splenic function or to a toxic effect on the bone marrow analogous to that which produces the arthritis. *M. Baker.*

On So-called Allergic Arthritis Symptoms. [In English.] APPLEGREEN, A. (1947). *Ann. Med. intern. fenn.*, **36**, 5.

A Practical Hypothesis for Chrysotherapy. COKE, H. (1947). *Rheumatism*, **3**, 126.

Physical Medicine in the Care of Rheumatoid Arthritis. POLLEY, H. F. (1947). *Sth. med. J.*, **40**, 596.

(Osteo-arthritis)

A Contribution to the Surgical Treatment of Osteo-arthritis of the Hip-joint. A Clinical Study. [In English.] GADE, H. G. (1947). *Acta chir. Scand.*, **95**, Suppl. 120.

The author performed 130 operations between 1938 and 1946 on a series of 115 patients with osteo-arthritis of the hip-joint. Three patients died, of pulmonary embolism, fat embolism, and paralytic ileus respectively.

The object of the monograph is to make a comparative evaluation of the various operative methods employed, and to describe the indications for them. The role of the joint capsule in the symptomatology of osteo-arthritis and the therapeutic value of joint-capsule extirpation in the operative treatment are dealt with. There is a chapter describing the methods of examination and the manner in which the clinical findings were recorded, including a new procedure for the registration of the functional value of mobility in the hip-joint. A detailed account is given of the therapeutic results obtained, and postoperative complications are discussed. In his last chapter the author makes a comparative evaluation of arthrodesis and arthroplasty on the basis of his own experience, and gives his view on the indications for these two types of operation.

The monograph is unsuitable for abstracting, and should be read in full by those interested. It is illustrated with radiographs, and case reports are presented in detail. There is a comprehensive bibliography.

Arthrodesis of the Hip by a Screw. (L'arthrodèse de la hanche par vissage.) CASUCCIO, C. (1947). *Rev. Orthopéd.*, **33**, 78.

The standard operation at present recommended for arthrodesis of the hip consists of a simple "blind" transarticular insertion of the screw without exposure of the hip-joint, followed if necessary by a subtrochanteric osteotomy to correct any deformity. The "blind" operation has now been performed 25 times for uncomplicated osteo-arthritis and 4 times for osteo-arthritis associated with unreduced congenital dislocations. In addition there have been 10 cases in which screwing has been used as part of an intra-articular arthrodesis and in which rapid and satisfactory bony fusion was obtained. Of the 25 patients submitted to arthrodesis by means of a screw alone, 18 have been followed up for more than

6 months. The other 7 are too recent. Of the 18 joints, 16 have a solid ankylosis, 12 of them being ankylosed in good position, and 4 are somewhat flexed and adducted. In 12 cases bony fusion of the hip appears to have occurred. *D. Ll. Griffiths.*

(Spondylitis)

Excretion of 17-Ketosteroids in Ankylosing Spondylarthritis and in Rheumatoid Arthritis: A Preliminary Report. DAVISON, R. A., KOETS, P., and KUZELL, W. C. (1947). *J. clin. Endocrinol.*, 7, 201.

An investigation of the 17-ketosteroid output in the urine of patients with ankylosing spondylitis is described. In 13 male patients an average excretion of 27·3 mg. in 24 hours was found, with a range of from 19·2 to 43·7. The average value is somewhat high for the group (the average for normal males is 14 mg.). This is contrasted with the findings in 11 female patients with rheumatoid arthritis who excreted an average of 12·8 mg. in 24 hours, with a range of from 3·5 to 21·6 (average for normal females 10 mg.). It is suggested that this point requires further investigation, since ankylosing spondylitis has such a predominating male incidence. *E. F. Scowen.*

Eosinophilia in Spondylitis Ankylopoietica. (Die Eosinophilie bei Spondylarthritis ankylopoietica rheumatica.) BÖNI, A. (1947). *Schweiz. med. Wschr.*, 77, 647.

Eosinophilia is often observed in the early stages of spondylitis ankylopoietica. The number of eosinophils varies between wide limits, as shown by specimen curves from 4 patients. Of 14 patients, 8 showed marked eosinophilia at the end of their first course of treatment, while in 6 cases the count was normal. The erythrocyte sedimentation rate curve shows deviations similar to, but not parallel with, those of the eosinophil count. The appearance of a constant eosinophilia usually heralds the onset of subjective and objective improvement in the patient's condition, even though the sedimentation rate may remain high. In the chronic stage of the disease the appearance of eosinophilia may again foreshadow improvement in the condition, although the latter may be preceded by temporary exacerbation of the disease process. *S. S. B. Gilder.*

Spondylarthritis Ankylopoietica. (Aspects actuels de la spondylarthrite ankylosante.) COSTE, F., MOUZON, M., and BOISSIÈRE, H. (1947). *Bull. Soc. méd. Hôp. Paris*, 63, 493.

A review is made of 76 cases of spondylarthritis ankylopoietica; 1 patient was a female. This disease seems to have become commoner recently and, while the chief features remain unchanged, the peripheral joints appear to be more frequently involved (60% of cases); in more than a quarter the involvement was serious. Radiological examination showed most evident changes in the dorso-lumbar region. The erythrocyte sedimentation rate was raised in 85% of cases; in the majority of those in which the rate was normal the condition was not progressive. In only 2 cases was there a family history of spondylarthritis ankylopoietica, but in 12 others a member of the family had suffered from some form of rheumatism. The condition was seen in 14 patients who had been prisoners of war or who had been deported for forced labour; it is suggested that the rigorous conditions of life were aetiological factors. *T. G. Reah.*

The Orthopaedic Treatment of Spondylarthritis Ankylopoietica. (De orthopaedische behandeling van spondyarthritis ankylopoietica.) KUIPERS, R. K. W. (1947). *Ned. Tijdschr. Geneesk.*, 91, 851.

After a survey of the orthopaedic treatment of patients with ankylosing spondylitis already showing malformation of the spinal column, the author describes a corset designed to correct the malformations. Only when the corset fails to give the desired results should operative treatment be considered.

Spondylolisthesis. A Clinical and Radiological Study based on 70 Personal Cases. (Le spondylolisthesis. Étude clinique et radiologique d'après 70 observations personnelles.) SÈZE, S. DE, and DURIEU, J. (1947). *Sem. Hôp. Paris*, 23, 1551.

Osteosclerotic Spondylopathy. (Le spondilopatie osteosclerotiche.) FERRERI, L. (1947). *Radiologia, Roma*, 7, 495.

Spondylitis in Brucellosis. (Espondilitis brucelósica.) VILLAFAÑE LASTRA, DE T., FAURE, J. G., and BERGOGLIO, R. (1947). *Medicina, B. Aires*, 7, 308.

(Miscellaneous)

Surgical Treatment of Degenerative Arthritis of the Knee Joint. HAGGART, G. E. (1947). *New Engl. J. Med.*, 236, 971.

Conservative treatment in unilateral degenerative arthritis of the knee-joint was found to be so disappointing in the Lahey Clinic, Boston, that in 1940 a plan of surgical management was evolved in certain selected cases.

The operation requires that the patient's physical condition should be good, that he should be prepared to co-operate in tiresome and painful exercises in convalescence, and that he should be eager to return to normal activity.

This article is based on the results of operation on 35 patients whose average age was 57; of all the cases seen these few were suitable for operative procedures. Five patients with advanced degenerative arthritis had an arthrodesis. Postoperative fixation was obtained by a long leg plaster cast for 2 weeks; this was followed by a Stader unit for 6 to 8 weeks, and then a further long leg plaster cast which allowed the patient to walk and was maintained until radiographs showed that union was sufficient. Finally a long leg caliper was fitted until fusion was firm. The result was excellent in all cases.

A designed arthrotomy was carried out through a midline incision in 30 cases. Its object, as defined by Magnuson, was the complete removal of all mechanical irritants from the joint. The patella was either removed or lessened in size. Hypertrophied synovia and pads of fat were removed from the anterior compartment. Degenerated articular cartilage and exostoses were shaved away as well as the menisci, if involved. Exercises

were started on the third day after operation and weight-bearing was allowed within 2 weeks. It was found that a manipulation under " pentothal " anaesthesia within the third week in 3 out of 4 patients hastened recovery. Three patients did not co-operate and the results were poor. In 12 the results were excellent, but 8 patients still complained of aching pain with changes in the weather and 7 of mild discomfort on starting activity after rest. There was no change in later radiographs compared with those taken immediately after operation.

[To be successful conservative treatment must be initiated as early as possible in arthritis. It must be regular, prolonged, and vigorous, with the object of overcoming quadriceps wasting and securing a greater range of movement. The patient may have to be rested from weight-bearing for a period during treatment, and manipulation, with or without anaesthesia, may be an important part of treatment. Improvement is not, however, maintained in some patients in spite of this, and in certain selected cases from this group operative procedures such as are recommended in this article are indicated.] *W. E. Tucker.*

Gonococcal Rheumatism Greatly improved by Aneurine Alone. (Rhumatisme gonococcique très amelioré par l'aneurine seule.) COSTE, F., and BOISSIÈRE, H. (1947). *Rev. Rhum.*, **14**, 177.

Articular Osteochondromatosis. (Osteocondromatosi articolare. Due casi.) MUSANTE, C. (1947). *Infortun. Traumat. Lavoro.*, **13**, 41.

Osteochondritis Dissecans. An Analysis of Forty-two Cases and a Review of the Literature. LAVNER, G. (1947). *Amer. J. Roentgen.*, **57**, 56.

Gout

Treatment of Gout by Vitamin B_1. (Le traitement de la goutte par la vitamine B_1.) COSTE, F., GRIGAUT, A., and AUQUIER, L. (1947). *Sem. Hôp. Paris*, **23**, 312.

Of 32 patients with gout treated with aneurine, 18 derived marked benefit, since pain, stiffness, and objective signs disappeared; 10 improved slightly; 4 were not affected. The best results appeared to be obtained by combined oral and intravenous administration, the former preceding a combination of the two methods by several days. Oral dosage ranged from 20 to 30 mg. daily for 20 days; daily intravenous injections began with 10 mg., the dose being increased to 75 mg. and a course lasting for 8 to 11 days. No ill effects from the injections were observed, but 3 patients had exacerbations of their gout during treatment. The authors think aneurine should be used where colchicum treatment has failed.

H. B. Gilder.

An Approach to the Diagnosis and Treatment of Gout. BARTELS, E. C. (1947). *Bull. New Engl. med. Centre*, **9**, 86.

The authors emphasize that gout does not necessarily run hand in hand with wealth, obesity, and great eating and drinking; one-third of patients have never taken alcohol, and in less than half the initial attack starts in the great toe. Gout should be diagnosed from a history of attacks of acute arthritis in any of the joints of the extremities, lasting for a few days or weeks, and with complete remission. A cut-out shoe with no history of trauma, acute arthritis soon after operation, and non-specific olecranon bursitis are all suggestive of gout.

Acute attacks are best treated by colchicine, 1/100 gr., every hour for six to eight hours, limiting the diet to carbohydrates. Intravenous glucose (500 c.cm. of 20% solution) has been given daily in hospital with benefit. The interval treatment aims at lowering the uric acid in the blood by a diet low in purine and fat and high in carbohydrates, and by eliminating the uric acid by cinchophen or aspirin. Alcohol should be strictly forbidden as it may play a part in causing toxic manifestations from cinchophen. *T. G. C. Early.*

Two Observations of Atypical Gout. (Deux observations de goutte atypique.) WEIL, M.P., and POILPRE, E. (1947). *Rev. Rhum.*, **14**, 174.

Non-Articular Rheumatism

Ruptured Intervertebral Disc and Sciatic Pain. BARR, J. S. (1947). *J. Bone Jt. Surg.*, **29**, 429.

Though the ruptured disc is universally recognized as a cause of sciatica, careful investigation is still necessary for accurate diagnosis. The negative explorations in some cases may be due to the fact that a prolapse is so far lateral that it can only be uncovered by facetectomy; the surgeon may be in doubt whether to do this or to carry out spinal fusion. Localized backache may be the only symptom of a protrusion so small as to escape notice both at myelography and at operations. There are, however, many other ligamentous and postural causes of backache, and many needless laminectomies have been performed on patients with ankylosing spondylitis.

Neurological examination fixes the level of the lesion in only half the cases, and the author states that most American surgeons use myelography as a routine. He prefers " pantopaque ", which is aspirated after all the films have been taken, and in 90% of cases finds a correlation between radiographic and operative findings. Operation is reserved for intractable pain, for such gross features of root compression as paresis or sphincter disturbance, and for cases where conservative management has failed after 6 weeks. Though conservative treatment is varied, rest in bed during an acute attack with spine, hips, and knees slightly flexed is as good as any; the lower part of the back must be protected subsequently.

The author discusses the vexed question of whether spinal fusion should or should not be performed at the time of operation. In many cases it seems obvious that existing lumbar instability and the results of operative trauma call for the fusion of the adjacent vertebrae. On the other hand, some neurosurgeons maintain that fusion is rarely, if ever, indicated; this may be because they pay more attention to the relief of sciatica than to the subsequent condition of the back. Certainly, whenever a facetectomy has been done, fusion must be performed also or disabling symptoms may result. The author's view is that, since there is an even chance of chronic back symptoms developing after simple exploration, it is logical to carry out fusion in every case, provided the technique neither raises operative risks nor prolongs convalescence. Such a technique is available in the notched " clothes-pin " graft of Bosworth. This is taken from the ileum and wedged between the fourth lumbar and first sacral spinous processes, which are held widely apart in acute flexion so that the graft is firmly

locked when the spine is again extended. A simple brace is all the postoperative immobilization needed, and patients are discharged from hospital in 4 weeks.

A questionary sent to 234 patients, 102 of whom had had a spinal fusion, revealed a modern but definite superiority of end-results in the fused cases. This was true not only as regards backache, stability, and capacity for exertion, but in respect of the root-irritation symptoms. The results in industrial accident cases were below average, and psychoneurotic complications were frequent; surgery should not, however, be withheld for these reasons. *David Le Vay.*

The Disc Factor in Low Back Pain with or without Sciatica. LOVE, J. G. (1947). *J. Bone Jt. Surg.*, **29**, 438.

The prolapsed disc is stated to be the commonest intraspinal cause of sciatic pain, and a conventional account is given of the clinical features. History and orthopaedic examination are usually conclusive. Neurological examination, though it must always be made, is not only not essential to the diagnosis but is of little value in locating the lesion. It may be confusing—for example, when a dermatome corresponding to a higher segment is involved through compression and ascending oedema of the cauda equina. The author advises routine myelography and personally favours introduction of oxygen or air as least irritant, though also least accurate. The simplest possible operative exposure is advocated, by unilateral reflection of the erector spinae, and excision of the ligamentum flavum, with removal of bone only where the interlaminar space is very narrow. The entire disc is not removed at the Mayo Clinic. A combined operation, in which the neurosurgeon removes the protrusion and the orthopaedic surgeon fuses the last two lumbar vertebrae to the sacrum, is desirable in many cases. However, the author does not consider that grafting should be a routine; not only may gross prolapse recur beneath a sound fusion but the extra stress imposed at the third space may cause a lesion at this level.

At the Mayo Clinic between 1939 and 1941 four neurosurgeons performed 1,217 operations with only 3 deaths; in 12% of patients the combined procedure was carried out. A follow-up of 987 showed that there was complete relief of pain in 53·7% and partial relief in 36·7% after simple removal of a protrusion. Nevertheless 35 to 40% still experienced aching in back or leg, and the same proportion were unable to continue their original occupation. The overall result was that 90·4% of patients had been relieved to some extent by operation, and 93% answered the frank question " Has the operation been worth while ? " in the affirmative. Prolapse recurred in 47 at the original level, and many of these cases were resistant to any form of further treatment. *David Le Vay.*

Pathological Studies of Intervertebral Discs. ECKERT, C., and DECKER, A. (1947). *J. Bone Jt. Surg.*, **29**, 447.

This is a report on the histology of the specimens of discs removed at laminectomy in 166 patients, compared with control material obtained at necropsy. The changes observed were not essentially different from the normal effects of ageing seen in the controls. These included nuclear prolapse into the cartilage plate with vascularization of the extension; scarring of nucleus and annulus; and granular degeneration of the nucleus with patchy calcification, presumably the sequel to desiccation. No relation seemed to exist between histology and clinical end-results. *David Le Vay.*

An Analysis and Differentiation of Low-Back Pain in Relation to the Disc Factor. STEINDLER, A. (1947). *J. Bone Jt. Surg.*, **29**, 455.

The author believes that the intact intervertebral disc has few sensory fibres and gives rise to little pain. It is one of the first structures to undergo senescent change. Simple thinning and collapse cause relaxation of the ligamentous connexions of the adjacent vertebrae and re-alignment of the intervertebral joints. Thus, recurrent lumbo-sacral strain may result from new stresses on ligaments and muscles before any actual herniation has occurred; at the same time, reactive hypertrophic arthritis may produce root symptoms by encroaching on intervertebral foramina. Herniation itself is a continuous process, and an originally mobile protrusion capable of spontaneous reduction may become fixed and adherent to nerve roots. Recurrent exacerbations are probably due to gross oedema of the fragment.

In diagnosis, neurological signs are a sufficient and desirable proof of the existence of a disc prolapse. In their absence it is advisable to seek a trigger-point and to see if procaine injection abolishes the referred pain; should this be the case, no disc lesion exists.

Laminectomy is indicated once the diagnosis is certain; fusion is essential whenever backache is a prominent feature of the history, and should preferably be performed as a routine. However sparing of bone the laminectomy may be simple removal of the prolapse cannot relieve lumbo-sacral instability which exists before the operation. The Bosworth " clothes-pin " method of fusion is a good one. *David Le Vay.*

Lumbago, Sciatica, and Endocrinology: Heterotopic Endometriosis. (Lombo-sciatalgie et endocrinologie. Contribution à l'étude des endométriomes hétérotopiques.) DAGNELIE, J. (1947). *Ann. Endocrinol.*, **8**, 26.

A woman of 32 gave a long history of pain in the back and along the distribution of the sciatic nerves; the pain had disappeared during a pregnancy and reappeared 6 months afterwards. It was worse during the follicular phase of the menstrual cycle and had been greatly aggravated by an injection of follicular hormone. A thorough investigation revealed two extremely tender nodules in the pelvis. Pressure on one of these provoked pain along the back of the left leg. A 9-months' course of testosterone (10 mg. four times a month) was given with complete relief from pain after the first injection. When the injections were temporarily stopped the pain returned within 3 months; further injections caused it to disappear again. The pelvic nodules have become smaller and less tender. It is assumed that the cause of pain was pressure on nerves by nodules of heterotopic endometrium. *S. S. B. Gilder.*

Low Back Pain Associated with Varices of the Epidural Veins Simulating Herniation of the Nucleus Pulposus. EPSTEIN, B. S. (1947). *Amer. J. Roentgen.*, **57**, 736.

Three cases of low back pain associated with epidural varices are reported. In 2 the diagnosis of prolapse of an intervertebral disc was made on clinical and myelographic evidence, in the third on clinical evidence alone. All 3 patients had a history of trauma preceding the onset of the low backache. The pain, which in 2 of the cases was made worse by coughing and sneezing, radiated down the leg on the affected side. Sometimes the pain was prolonged and severe. Changes in the ankle-jerk

and knee-jerk were present in 2 cases, and in 1 there was atrophy of the leg and thigh. The total protein content of the spinal fluid was raised in 2 of the patients and was close to the upper limit of normal in the third case. Radiographs showed no abnormality. Myelography with " pantopaque " revealed defects at the level of the sacro-iliac disc in 2 cases, and these were interpreted as due to prolapse of the disc.

The paper discusses the anatomy of the epidural veins and the differentiation of the myelographic appearances in dilated epidural veins and in varicosities of the pial veins. Whereas in cases of dilated epidural veins the myelographic picture is indistinguishable from that of a prolapsed disc, dilated pial veins are enveloped by the pantopaque, and channel-like radiotranslucent shadows are produced where the opaque oil is displaced by the dilated veins. *A. Orley.*

Laminectomy and Foraminotomy with Chip Fusion. Operative Treatment for the Relief of Low-back Pain and Sciatic Pain Associated with Spondylolisthesis. BRIGGS, H., and KEATS, S. (1947). *J. Bone Jt. Surg.*, **29**, 328.

The authors draw attention to the fact that the symptoms of backache and crural pain in patients with spondylolisthesis are not always completely relieved by spinal fusion. They have tried to devise an operative procedure which will not only stabilize the spine but also afford lasting relief of pain. They believe it essential to explore the intervertebral disc in all cases; in those with radiating pain exploration of the nerve roots is necessary as well. *R. Furlong.*

Choice of the Best Operative Method in Sciatica due to Disk Lesions, on the Basis of Late Results. (Le choix de la meillure méthode opératoire dans les sciatiques d'origine discale d'après l'etude des résultats éloignés.) PETIT-DUTAILLIS, D., and PERTUISET, B. (1947). *Mém. Acad. Chir., Paris*, **73**, 396.

During the last five years the authors have modified their technique for the treatment of sciatica due to disc lesions, because of the fairly frequent occurrence of homolateral lumbar pain or contralateral sciatica after simple removal of the disc. They now decide at operation whether or not a prolapsed disc is responsible for symptoms. If it is not, bilateral rhizotomy is undertaken of L5 and S1. The results in 17 cases were: perfect, 2; very good, 6 (slight persistent coccygeal pain or vasomotor disturbance in the leg); good, 7 (some persistent lumbar pain, paraesthesiae, or vasomotor disturbances in the legs); failure, 1; recurrence, 1.

For sciatica due to prolapsed disc they advise removal of the disc together with rhizotomy of L5 or S1 (unilateral or bilateral), but not both of these roots; in 28 patients so treated there were 12 perfect results, 8 very good results, and 5 results marred by residual pain after prolonged effort or by contralateral sciatica; the results were mediocre in 3 patients, there being persistent lumbar pain or paraesthesiae. In a total of 250 disc operations prolapse has only recurred 7 times; prolapse of another disc has occurred 3 times.

After rhizotomy of both L5 and S1 paraesthesiae and even trophic lesions may be disturbing, though not really severe. Anaesthesia extends over the lower half or two-thirds of the antero-lateral and postero-lateral aspects of the leg, the retro-malleolar fossa as far as the heel tendon, the lateral half of the dorsum of the foot and the lateral third of the sole, and the dorsal and plantar aspects of the three lateral toes. Sometimes the anaesthetic area includes the first and second toes, and it may extend proximally over the postero-lateral aspect of the knee or even as far as the gluteal fold.

Cutting the first sacral root causes anaesthesia or hypoaesthesia along the lateral border of the foot and adjacent parts of dorsum and sole, the two lateral toes, the lateral retro-malleolar sulcus, and the lowest part of the postero-lateral aspect of the leg. Proximally the anaesthesia sometimes extends over the upper part of the leg, the knee, or even the thigh, in their lateral aspects. Fifth lumbar rhizotomy usually produces a vertical band of anaesthesia on the antero-lateral aspect of the leg, often extending to the plantar and dorsal aspects of the great toe or the first two or three toes. A certain number of rhizotomies are followed by paraesthesiae, vasomotor effects, and either hyperhidrosis or anhidrosis. Trophic disturbances are exceptional, but were observed in one case of rhizotomy of both L5 and S1. Rhizotomy of a single root, even if bilateral, is tolerated; rhizotomy of both L5 and S1 may be followed by effects which, though not serious, are none the less appreciable, and the operation should be resorted to only if a cure cannot be obtained by other means. In sciatica due to prolapsed disc it is reserved for the treatment of recurrence of pain without obvious recurrence of prolapse.

Some of the recurrences in this series seemed to be due to persistence of " lipiodol " within the nerve roots; as far as possible lipiodol examination is dispensed with in diagnosis. *Ian Aird.*

Operative Results in Intervertebral Disks. GRANT, F. C. (1946). *Ann. Surg.*, **124**, 1066.

The author points to the paucity of postoperative follow-up reports in cases of lumbar disc protrusion and quotes a number of published series. He points out that the pain has two components, pain in the back being due to pressure upon or rupture of the posterior vertebral ligaments, and pain in the leg to protrusion of the disc against the adjacent nerve roots. Maybe the back pain points to a structural disability of the back which later gives rise to the protrusion. The author's own contribution deals with the results of surgical removal of an abdominal disc in 200 cases with a follow-up period of 6·5 to 1·5 years (average 3 years). A questionary was sent out to 275 patients; 200 replied and 150 reported in person. In this series 63% were completely relieved of all pain, 29% were improved, and 8% were unimproved or worse. The results were not affected by the occupation of the patient, being apparently the same in those doing heavy manual work as in those of sedentary occupation. The degree of the protrusion had a bearing on the results, these being best with the ruptured disc, less good where the annulus protrudes without rupture, and least good in cases of the so-called " hidden " disc.

The author also analyses two other groups of cases. Of 29 cases in which no disc protrusion was found at operation the results were approximately the same as those which followed removal of " hidden " discs. Of 44 cases in which the diagnosis of a disc protrusion was made and operation was not performed, 23% underwent spontaneous cure and 41% were considerably improved. He concludes by urging caution upon those who are prepared to operate when the diagnosis of a lumbar disc protrusion has been made without assessing the severity of the patient's pain or considering its duration and the number of previous attacks. *J. E. A. O'Connell.*

The "Last-straw" Factor in Low Back Disability. With Summary of 100 Cases Examined and Evaluated by the Medical Advisory Board of the Industrial Commission of Arizona, 1934–1943. WATKINS, W. W. (1947). *Radiology*, **48**, 20.

This report is based on 100 cases examined and evaluated by the Medical Advisory Board of the Industrial Commission of Arizona in 1934–43. The author points out the difficulty in assessing the compensation for injuries, alleged or real, sustained by workers whose radiographs immediately after an accident show evidence of developmental anomalies or pathological changes. He considers that, while such conditions as rheumatoid arthritis produce clinical signs before radiographic changes, osteo-arthritic changes are usually symptomless long after they are radiologically evident. A workman with either of these conditions who sustains an injury may well be disabled for a long time, and serial radiographs show progressive development of the pathological processes. The assessment of compensation for this "last straw" damage is much more difficult than is suggested by the awards of the Medical Advisory Board.

J. F. Brailsford.

Fibrositis. MOWBRAY, J. (1947). *J. med. Ass. Eire*, **21**, 8.

The main theme of this article is that fibrositis, the commonest form of the rheumatic conditions, has become amenable to treatment owing to recent and brilliant researches upon its aetiology. Stockman in 1920 described the histology of a typical nodule as first an exudation of fluid with lymphocytes, and next becoming organized by invasion with fibroblasts and blood vessels which were finally almost obliterated by the appearance of dense connective tissue; but it was left to Sir Thomas Lewis and later Kellgren to show that pain originating in muscular foci yielded to injections of procaine, clearing up by this method many cases which had remained stubborn to physical methods. When procaine injections into an area remove the pain, tenderness, and stiffness, several factors are probably at work—the bulk of the fluid breaks down adhesions, and the immediate relief of spasm and pain on movement encourages the patient and thereby helps to abolish "habit-spasm".

The diagnosis is helped by noticing whether active and passive movements are each painful in the same direction, in which case the structure at fault is probably a ligament or other inert body; or whether active movement is painful in one direction, and passive movement in another, when the site must be in muscle or tendon. Fibrositis is found not only in muscle, tendon, and bursa, but can involve the capsules of joints, both primarily or secondary to rheumatoid and osteo-arthritis—the former showing itself as a painful, tender, but not swollen joint accompanied by muscular wasting with no radiological changes and a normal sedimentation rate.

As for focal sepsis, eradication may well improve the patient's general condition but is unlikely to cure the local fibrositis.

The importance of developing sensitive fingers which will feel the slight spasm of muscle is emphasized.

T. E. C. Early.

The "Costoclavicular Syndrome". TELFORD, E. D., and MOTTERSHEAD, S. (1947). *Brit. med. J.*, **1**, 325.

The causes of symptoms of pressure on the neurovascular bundle in the region of the thoracic inlet are discussed in relation to: (1) operation findings in 120 cases; (2) investigation of the effects of posture on the radial pulse in 120 healthy medical students; and (3) dissection of 30 bodies. Of the operation cases, 14 showed extensive arterial thrombosis, and in these there was a well-developed cervical rib. In no case, however, was any abnormality found in the artery in the region of the rib. Indeed, in only 2 cases did the thrombosis extend above the level of the lower border of the pectoralis major. Of 104 uncomplicated cases, 69 showed some degree of cervical rib; in 12 there was a strong taut band arising from the tip of a small cervical rib, and passing downwards and forwards in the anterior border of the scalenus medius; 8 showed a condition in which the insertion of the scalenus medius was carried forward further than normal.

Diminution or arrest of the radial pulse can be produced by certain positions of the shoulder girdle. This is due to compression of the axillary artery below the clavicle and not, as is frequently stated, of the subclavian artery. Adduction of the arm against resistance was most effective in interfering with the radial pulse, producing complete arrest in 66% of cases.

In 12 out of 18 dissections made with the arm by the side of the body a sharp S-turn was found in the axillary artery at the level of the second rib. At this point the artery was embraced in a scissors-like manner by the heads of the median nerve, which were seen to constrict the vessel on depression of the shoulder. This constriction was demonstrated directly in one case at operation. It is suggested that obliteration of the pulse in forcible adduction of the arm may be due to compression of the axillary artery by the pectoralis minor and subscapularis. In no case did dissection afford any support for the belief that symptoms may be due to compression of the brachial plexus between the clavicle and the first rib when the shoulder is depressed. Clavicular pressure may occur in retraction and abduction of the shoulder; but usually the symptoms are due to kinking of the brachial plexus over a cervical rib, a band, the scalenus medius, or an abnormal first rib when the shoulder is depressed. Vascular disturbances are due to causes distal to the clavicle and have nothing to do with the costo-clavicular syndrome.

A. Barer.

The Supraspinatus Syndrome. ARMSTRONG, J. R. (1947). *Lancet*, **1**, 94.

The supraspinatus syndrome is a frequent cause of shoulder pain, often overlooked. The lesion may be a small tear in, or a tendinitis of, the supraspinatus tendon, or a subacromial bursitis, produced by injury of the abducted upper limb; symptoms are caused by impingement of the affected tendon and/or bursa against the acromion process in the middle range of abduction of the shoulder joint.

In 31 patients submitted to operation the pathological macroscopical findings were: (a) inflamed thickened bursal wall with a red thickened underlying tendon (15 patients); (b) calcified deposits in a thickened bursa and tendon (6); (c) tears of the supra spinatus tendon (5); (d) bursitis, difficult to distinguish from bursitis with tendinitis (5). Most patients gave a history of injury, the injury being followed, immediately in the patients with a tear of the tendon and later (12 to 24 hours) in those with a contused tendon and bursa, by pain referred to the insertion of the deltoid muscle; a painful arc on abduction of the shoulder-joint between 60 and 120°; a reversed scapulo-humeral rhythm; and tenderness localized to the subacromial bursa. Later there might be periarticular adhesions due to lack of use of the shoulder

producing true limitation of movement. The syndrome may be confused with: (1) complete rupture of the supraspinatus tendon, but in the latter condition there is loss of ability to abduct the shoulder-joint; (2) "frozen shoulder", where there is generalized stiffness of the joint with much pain on forced movement; (3) tuberculous arthritis of the shoulder-joint, which should be distinguished by muscle spasm and wasting, by pain at the end of the joint movements, and by the *x*-ray appearances. Fibrositis and neurosis are frequently diagnosed where the supraspinatus syndrome exists.

Of 89 patients suffering from supraspinatus syndrome, 58 recovered with conservative treatment—rest of the upper limb in a sling rather than in an abduction splint for 1 week followed by active shoulder exercises. Infiltration of the tender area with local analgesic, radiant heat, and short-wave diathermy were used, but the author considers that improvement obtained by these measures was temporary. In the remaining 31 patients conservative measures failed; accordingly removal of the acromion through an antero-posterior "sabre cut type" incision over the region of the acromio-clavicular joint was performed. The whole acromion, including the articular surface of the process at the acromio-clavicular joint, needs to be removed, otherwise there is danger of incomplete relief of symptoms due to removal of insufficient bone. This happened in 5 of the first 9 patients submitted to operation; 3 were again operated on with complete relief of symptoms. Postoperatively, the limb is rested in a sling by the side of the body for 1 week; this is followed by active movements. In about 3 to 4 weeks, according to the author, movements are full. [This statement seems optimistic.]

The author admits that he is unable at the onset of treatment to determine which patients will require excision of the acromion; in his experience, however, the operation is indicated where: (a) supraspinatus syndrome "causing material disability" is associated with calcified deposits in the tendon; and (b) a supraspinatus syndrome with disability is not cured by conservative treatment in 2 to 3 months. The operation should not be performed where there is true limitation of movement of the shoulder-joint due to periarticular adhesions; these should be dealt with first by physiotherapy, and if necessary by manipulation.

[This article would have been of greater value if the author had followed up his cases and had been able to present end results after, say, 3 or 5 years.]

David Trevor.

Causalgia. A Report on 32 Cases. PASRICH, H. R. (1946). *Indian med. Gaz.*, **9**, 337.

This article describes 32 cases of causalgia in Indian troops. Mitchell's original criteria have been followed, and a pain classified as causalgic only if it was: (a) in the region of a peripheral nerve subjected to damage; (b) spontaneous; (c) continuous; (d) liable to exacerbation; and (e) burning. Causalgic pain followed injury within 7 to 10 days; pain occurring more than 3 weeks later was looked upon with suspicion. The incidence was 2% in peripheral nerve injuries with a preponderance in Gurkhas; it is thought that, because in Gurkhas there is a tendency to keloid formation, they are especially liable to intraneural fibrosis. Support for this view is adduced from the fact that, after the general use of penicillin in the forward areas, infection of the wounds and subsequent scarring was reduced and the incidence of causalgia fell. Of the 19 cases of median nerve causalgia, 4 showed no signs, motor or sensory, of damage to any of the nerves of the limb, and 7 showed complete anaesthesia in the area affected by the causalgia. Ischaemia due to concomitant damage to the blood vessels was negligible. The pain always began in the same area of the limb—that is, in the lateral half of the palm of the hand and in the sole of the foot. The conclusion is that the focus of irritation lies in the intraneural fibrosis affecting the central fibres of the nerves, and impulses from this focus set up changes in the spinal or thalamic centres. Before treatment was begun an injection of procaine was given into the sympathetic ganglionated cord. Four cases yielded to repeated injections, but periarterial sympathectomy was performed in 3 cases, and section of the ganglionated cord in 21. All the sympathectomies gave dramatic results except in a man who lost his pain but had hyperaesthesia for 3 months afterwards. *H. T. Simmons.*

Rheumatic and Syphilitic Juxta-articular Nodes. (Rheumatische en luetische knobbels bij de gewrichten.) DIJKSTRA, O. H. (1947). *Ned. Tijdschr. Geneesk.*, **91**, 1299.

A biopsy of subcutaneous nodules in the region of the elbow-joint was made in two cases of chronic rheumatism. The histological picture was one of connective tissue containing areas of degeneration sharply demarcated by a zone of connective-tissue cells. Exudate, principally of lymphocytes, was scanty. The same type of nodule was found in a third case without evidence of rheumatism.

Comparison is made with the nodules found in yaws and syphilis, on the basis of four specimens. These nodules, which like the rheumatic nodules may attain the size of a walnut, are not so strictly juxta-articular as the former and contain more exudate, usually with plasma cells present. An arrangement of concentric layers can often be distinguished. Photomicrographs are reproduced. *H. B. Gilder.*

Sciatica and the Intervertebral Disc. JACK, E. A. (1947). *Rheumatism*, **3**, 122.

Sciatica and "Blocked" Septic Foci. (Ciática y foco séptico bloqueado.) FERRERO, R. G. A. (1947). *Rev. argent. Rheumatol.*, **12**, 127.

Sciatica, with particular Reference to its Causes and Treatment. ROGERS, L. (1947). *Post Grad. med. J.*, **23**, 517.

Surgical Treatment in Cases of Chronic Rheumatism. (Aké sú možnosti chirurgickej terapie chronického reumatizum.) CERVEŇAŇSKÝ, J. (1947). *Slov. Lek.*, **9**, 195.

Myalgia and Fascialgia in Sciatica. (Myalgie en fascialgie bij ischias.) PEERAER, D. (1947). *Belg. Tijdschr. Geneesk.*, **4**, 66.

The Importance of Diet in Chronic Rheumatism. MILLES, H. L. (1947). *Med. Pr.*, **128**, 345.

Chronic Rheumatism in the Hand and Neurotrophic Rheumatism of the Upper Limb. (Rhumatismes chroniques de la main et rhumatisme neurotrophique du membre superieur.) RAVAULT, P. P., GUINET, P., BERTHIER, L., EMERY, —, and CARRIER, P. (1947). *J. Méd. Lyon*, **657**, 363.

General Articles

Rheumatism. O'REILLY, T. J. (1947). *J. med. Ass. Eire*, **21**, 2.

Although the history of rheumatic diseases is long, it was not until Heberden in 1805 described the nodes which bear his name that any useful knowledge began to accumulate; Heberden pointed out that these pea-like tumours near the joints of the fingers " have certainly nothing in common with gout, for they are found in many patients who have no experience of that disease ".

The social changes which occurred in Germany at the end of the nineteenth century, and in England in 1911, with social insurance, free medical treatment, and certification to control the treatment, showed up the extent of the illness due to rheumatism. Much organized treatment and research was carried out—the latter yielding few results until recently in the case of fibrositis. The importance of the latter is emphasized by the figures of the first 5,000 patients attending the Dublin rheumatism clinic—of whom 70% suffered from fibrositis, 18·5% from osteo-arthritis, 10% from rheumatoid arthritis, 1% from ankylosing spondylitis, and 0·5% from gout. There is no doubt that many cases show a marked hereditary factor; climate seems to play some part, in that two peak periods, one in the spring and one in the autumn are often noted, both bearing some relationship to two virus diseases—the common cold and influenza.

Most treatment takes the form of physiotherapy, either heat or massage. The one great discovery, that of gold injections in the treatment of rheumatoid arthritis, was made in 1928. Other methods, such as manipulation of joints, are finding their place. But rheumatism clinics, where treatment can best be carried on, are only feasible in densely populated countries with large cities. *T. E. C. Early.*

Arthritis in the Mediterranean Theatre of Operations. I. Incidence of Joint Disease—Clinical Description of Rheumatoid Arthritis. SHORT, C. L. (1947). *New Engl. J. Med.*, **236**, 383.

Strictly surgical conditions, such as the immediate effects of wounds on joints, bones, muscles, etc., have been excluded from this paper; but fibrositis (under all its names) has been included because it is often confused with arthritis, as has " psychogenic " arthritis. Rheumatic fever is considered only in the differential diagnosis.

The importance of arthritic diseases as causes of manpower loss is shown in several tables. Only three other classes of patient (neuropsychiatric, skin, and gastrointestinal) have an incidence greater than the arthritic amongst those admitted to the seventy-third station hospital from August, 1943, to April, 1945. Percentage of total admissions was 1·8 for arthritis. An estimate of the man-days lost through hospitalization for arthritis from January, 1943, to May, 1945, came to 275,000.

At the Army and Navy General Hospital at Hot Springs, Arkansas, the incidence of various types of arthritis based on 2,000 cases was as follows: rheumatoid, 34·3%; psychogenic 18·8%; fibrositis 13·6%; hypertrophic arthritis, 12·4%; gonorrhoeal, 1·4%; miscellaneous causes, 19·5%.

Patients with joint symptoms but no objective changes were found most frequently (40%) in the Mediterranean theatre; rheumatoid and hypertrophic arthritis followed with 25% each; and specific infective arthritis numbered less than 10%.

The average age for rheumatoid arthritis was 39 years 9 months, higher than that for either arthralgia (34/9) or hypertrophic arthritis (38/10). Over half these patients gave a history of previous attacks, mostly without complete remission. Generalized symptoms such as tiredness and loss of weight were common (87%), sometimes before the onset of arthritis; vasomotor instability such as cold feet, sweating, and motor weakness were also present. Articular swelling was almost invariable, though occasionally a diagnosis was made with only pain and tenderness in symmetrical joints. Laboratory tests were not helpful: the sedimentation rate was raised in only about half the cases, the white cell count was variable, and *x*-ray examination of the joints was usually negative. Most of the " specific " forms of treatment were left untried; only fever therapy was given a chance in a few cases. The results were not impressive, nor was much success gained by removing even obvious " septic foci ". Rest in bed, relief of pain and physical therapy were the chief treatments given.

Atypical rheumatoid arthritis comprised some 18% of cases; it often followed an infection (viz. of the upper respiratory tract), and affected several joints in asymmetrical fashion. Chemotherapy was tried, usually without effect.

Rheumatoid spondylitis was found in 20% of patients with rheumatoid arthritis in the Mediterranean theatre. Many men who undoubtedly had this disease fought through a campaign, and one parachutist made a number of jumps. *T. E. C. Early.*

Arthritis in the Mediterranean Theater of Operations. II. Clinical Description of Hypertrophic Arthritis, Arthralgia and Psychogenic Rheumatism. SHORT, C. L. (1947). *New. Eng. J. Med.*, **236**, 429.

Arthritis in the Mediterranean Theater of Operations. III. Clinical Description of Infectious and Other Types of Arthritis. SHORT, C. L. (1947). *New Eng. J. Med.*, **236**, 468.

The author continues his review of joint disease in the Mediterranean area.

A Coefficient of Severity in Rheumatic Diseases. (Un coefficient de gravité des affections rheumatismales.) MICHEZ, J. (1947). *Arch. Rhum.*, **7**, 66.

The author has devised a chart, reproduced in the article, in which marks can be assigned to the several features of the disease which he thinks relevant to an assessment of its gravity; the sum of these marks is the " coefficient of gravity ", which in his opinion is of service in judging the progress of a patient and in assessing the value of a particular treatment. The features to which marks are to be assigned are grouped under three heads: (1) the extent of the disorder: in this the several joints of the body are listed, with columns for marks according to the degree of pain, stiffness, decalcification, or synovitis, and deformity; (2) the activity of the disease process: here the criteria are E.S.R., pyrexia, and anaemia; (3) the degree of disability. The marks to be assigned to the various objective signs, in their several degrees, and to the other features of the case are indicated. *Kenneth Stone.*

Final Consideration on the Development of a Group of 721 Rheumatic Children. (Consideraciones finales sobre la evolucion de un grupo de 721 ninos reumaticos.) BARBATO, D. (1947). *Arch. Pediat. Urug.*, **18**, 116.

A statistic review of 721 cases of rheumatic disease in childhood seen during 4 years is given. The cases are grouped into the following 6 classes according to their clinical condition when first registered (numbers in brackets): (1) acute articular rheumatism without cardiac involvement (139); (2) rheumatism with cardiac involvement but no insufficiency (429); (3) cases suspected of rheumatism (muscular pains, joint pains, etc.) but without cardiac signs (84); (4) rheumatism with cardiac insufficiency (43); (5) chorea without heart signs (16); (6) chorea with heart signs (10). Classification on any grounds but clinical was not considered feasible.

Cases are divided into (a) dead (69), (b) survived, and kept under review for at least 4 years (359). In group (a) the causes of death were: cause unrelated to the heart condition, 6; cause unknown, 4; rheumatic heart disease, 59. Of these 59, 28 were originally registered in class 4; 29 in class 2, and 2 in class 1: 28 were girls, 31 boys. In 39 the illness began with the classic type of acute articular rheumatism. The greatest time between the beginning of the illness and death was 10 years, and between the beginning of cardiac insufficiency and death 6 years. In 41 the final clinical lesions did not involve the pericardium. At death the youngest was 5, the oldest 21 years, and the majority of deaths occurred at 10 years old.

In group (b) progress was noted by the change in the heart condition. Of 54 cases in class 1, 45 remained the same and 9 grew worse (i.e. cardiac signs appeared). In class 2 (237), 137 remained the same, 65 improved, and 35 grew worse. In class 3 (46), 29 remained the same and 17 grew worse. In class 4 (9) all improved. In class 5 (8), 4 developed heart lesions. In class 6 (5), 4 remained the same and 1 improved.

The authors do not claim to have been so thorough as some authors, but they feel that their statistics confirm that their classification was useful. One of their objects was to have a basis on which to launch their campaign for a social attack on rheumatic disease.

J. G. Jamieson.

Significance of Function in the Genesis and Development of Experimentally Induced Polyarthritis and Carditis. (Die Bedeutung der Funktion für Entstehung und Entwicklung experimentell hervorgerufener Polyarthritiden und Karditiden.) INGELMARK, B. E. (1947). *Acta med. Scand.*, **128**, 203.

Pathological changes in joints and adjacent tissues, and in the myocardium, were found in rabbits previously injected intravenously with a suspension of enterococci isolated from the faeces in a case of polyarthritis. A freshly prepared suspension (2 ml.) from growth on ascites-agar was injected into an ear vein; this was repeated after 48 hours and again after 96 hours, each animal thus receiving three injections. The animal was killed 5 weeks later.

The observations were carefully controlled; all experimental and control animals lived under identical conditions, apart from " training ". The following groups were studied: (A) animals submitted to training (compelled to undergo a measured amount of running exercise daily, by being placed in a cabinet whose floor was an endless moving belt) both before and after inoculation; (B) animals submitted to training for a period before inoculation only; (C) animals trained only after the last inoculation; (D) animals not trained at all. When the results were examined, training appeared to have exerted a remarkable influence.

The pathological changes found were thickening of the synovial membrane; foci of lymphocytes and plasma cells in synovial membrane, capsule, and periarticular tissues; enlargement of synovial villi with round-cell infiltration hyperaemia; synovial exudation; and cartilage destruction. There was no neutrophil exudation. In all control animals except one, round-cell infiltration of the myocardium was found, but the number of cell infiltrations per unit volume was found to be smaller than in the experimentally infected animals. No changes were found in the endocardium or epicardium. More joints were affected and the morbid changes were far more pronounced in groups A and B than in C and D. There was little difference between animals of groups C and D; some animals of group A showed rather more marked changes than any of group B. Control animals submitted to the same training showed no joint changes.

It would follow that training before inoculation is responsible for a more marked pathological reaction. Though it would appear that training is the cause of a lowering of resistance to experimental infection of the heart and joint tissues, the author is careful to point out that the conclusion cannot be held as true for all tissues and all animals, tissue resistance being affected by a very large number of factors. It is in harmony with the clinical observation that acute and chronic rheumatism affect joints in active use earlier and more frequently than those used less. *Kenneth Stone.*

Temperature Equalization for the Relief of Pain. An Experimental Study of the Relation of Thermal Gradients to Pain. WELLS, H. S. (1947). *Arch. phys. Med.*, **28**, 135.

Although heat increases blood flow, there is little evidence that deficient blood flow has anything to do with those types of pain that respond well to heat. The present observations are based on studies carried out on a normal subject (the author), but confirmation of important findings has been obtained from other subjects.

A metal " serrefine " (syringe-type artery clamp), when applied to a finger web, causes moderate pain, which is lessened or even abolished if hand and clamp are warmed in air and water. The same results are obtained when the circulation in the arm is stopped by the inflation of a sphygmomanometer cuff, so that the analgesic effect of heat is not in this case due to an increase in blood flow to the injured area. Warming the hand alone failed to relieve the pain if the clamped tissues were kept cool by dipping the projecting metal in water at the initial skin temperature of the hand. Similarly, the warming of larger areas of the body failed to relieve the pain. If the hand is maintained at its original temperature, warming the end of the clamp by dipping it in water at 34° to 37° C. relieves the pain, but it recurs if the clamp and clamped tissues are heated above 37° or 38° C., with an increase in its intensity if the warming is carried above 45° C. Above that point tissue is injured and pain occurs as a result.

Further experiments are described.

Roentgen Therapy in Arthritis, Bursitis, and Allied Conditions. POHLE, E. A., and MORTON, J. A. (1947). *Radiology*, **49**, 19.

This paper is part of a symposium on rheumatic diseases. The great majority of 100 consecutive patients

considered were suffering from osteo-arthritis. There was an additional group of 69 cases of subdeltoid bursitis. *X* rays were used in treatment, with a half-value layer of either 1·05 mm. copper or 2·4 mm. copper. The spinal areas were treated through an 8×20 cm. port (1 to 3 areas) and the smaller joints through 10×10 or 15×15 cm. ports. The spinal areas received three irradiations of 150 r (in air) on successive days, or three of 200 r on alternate days.

The authors conclude that the response to treatment is in all probability due to the non-specific analgesic effect. In the osteo-arthritis group, satisfactory relief was obtained in about 75% of cases. The aged and the severity of the disease are not reliable guides in prognosis. The possible psychological effect of treatment is not denied. The response to treatment of bursitis was good, with satisfactory relief in 84% of cases, in over half of which there was calcification before treatment. Especially good results were obtained in acute cases; in some of those with calcification the calcium deposit disappeared.

A. G. C. Taylor.

Plantar Neuromas, Morton's Toe. BICKEL, W. H., and DOCKERTY, M. B. (1947). *Surg. Gynec. Obstet.*, **84**, 111.

In the painful affliction of the foot which now goes by his name, Morton succeeded in obtaining cures by excision of the fourth metatarsophalangeal joint and the surrounding tissues, but he did not identify any precise pathological process. In 1893 Hoadley cured a case by resecting a small neuroma of the branch of the lateral plantar nerve to the fourth toe. The significance of this finding was not appreciated until 1940, when Betts again drew attention to this condition and the results of excision. The authors review their experience of 18 patients, 16 women and 2 men aged from 25 to 67 years; most were overweight. The pain was usually felt beneath the heads of the third and fourth metatarsals and the contiguous sides of the corresponding digits, though occasionally it spread to the neighbouring digits. Pain was sometimes paroxysmal at night, and paraesthesiae in the affected toes were common. In 16 cases there was a localized tender spot over the site of the neuroma, and firm pressure here with a blunt instrument gave rise to typical radiating pain and paraesthesiae. Operation was carried out on each of these patients, conservative treatment having failed.

Patients suffering from this type of pain are usually women and commonly wear small, high-heeled shoes. The 2 men in this series wore ill-fitting shoes. Trauma and weight-bearing appear to be prime causes, but the authors consider that the anatomy of the plantar and digital nerves is also partly responsible for the pathogenesis.

D. W. C. Northfield.

Reiter's Disease. HARKNESS, A. H. (1947). *Brit. med. J.*, **103**, 72.

The author defines Reiter's disease as a clinical syndrome characterized by non-gonococcal urethritis, bilateral conjunctivitis, arthritis (usually polyarticular), occasionally balanitis and keratodermia blennorrhagica. The condition, always venereal, has a relatively long incubation, runs a protracted course, and may recur after long periods of remission. Urethritis is usually of the Waelsch type, though some cases may have a profuse purulent abacterial discharge with pain and frequency. In the author's series conjunctivitis appeared 2 to 16 days after the discharge started, and polyarticular arthritis 1 to 6 days later. Keratodermia blennorrhagica occurred subsequently in 50% of cases. This syndrome has also been described in association with gonococcal urethritis, though in these cases there is often a mixed primary infection, and in staphylococcal septicaemia. However, confusion is most liable to arise from its more frequently reported association with bacillary dysentery. The author considers that Reiter's original case was of dysenteric origin, and notes that Feissinger and Leroy, in a study of an outbreak of dysentery in 1916, observed the same clinical syndrome in 4 of their cases. The arthritis in cases of this type is more commonly met with during convalescence than during the acute stage, and is more frequently monoarticular. It is suggested that cases be differentiated into those of dysenteric and of venereal origin, and that the term "Reiter's disease", or "dysenteric arthritis" be reserved for the former; the latter should be described as "non-gonococcal polyarthritis" or "the non-gonococcal syndrome".

A. Henderson Begg.

Treatment of Reiter's Syndrome by Gold Salts. WILLCOX, R. R., FINDLAY, G. M., and HENDERSON-BEGG, A. (1947). *Brit. med. J.*, **1**, 483.

This is a description of 2 cases of Reiter's syndrome in which gold therapy appeared to expedite recovery.

Milkman's Syndrome with Fissuring of the Skeleton. (Syndrome de Milkman et fissurations spontanées du squelette.) MONDOR, H., and LEGER, L. (1947). *J. Chir., Paris.* **63**, 85.

This is a careful study of Milkman's syndrome based on the 80 cases published so far by some 30 authors, and on 8 new observations. The syndrome is identified by the *x*-ray appearance of the bones. There are multiple, often symmetrical, transverse bands of translucency in many of the long and flat bones of patients who come for examination because of "rheumatic" pain (worse on movement) and general weakness.

L. Michaelis.

Osteomalacia with Looser's Nodes (Milkman's Syndrome) due to a Raised Resistance to Vitamin D Acquired about the Age of 15 Years. MCCANCE, R. A. (1947). *Quart. J. Med.*, **16**, 33.

The original of this most important article on Milkman's syndrome should be consulted, since no précis can be adequate.

Penicillin Treatment of Rheumatism. (Pénicillinothérapie des rhumatismes.) COSTE, F., and GALMICHE, P. (1947). *Bull. Soc. méd. Hôp. Paris*, **63**, 503.

The authors record the results of treatment with penicillin of 163 cases of rheumatism, which include 84 cases previously reported (*Sem. Hôp. Paris*, Nov. 7, 1946).

Sudeck's Syndrome in Trivial Injuries. (Zur Frage des Sudeckschen Syndroms bei Bagatellverletzungen.) NICOLE, R. (1947). *Radiol. clin., Basel*, **26**, 93.

The author believes that wherever Sudeck's atrophy follows a trivial injury the triviality of the latter ought to be doubted, a thorough radiographic examination made, and treatment adjusted accordingly.

L. Michaelis.

BOOK REVIEWS

Chronic Structural Low Backache. By R. A. Roberts, B.Sc., M.B., Ch.B., D.M.R.E. 1947. H. K. Lewis. London. Pp. viii and 105; 137 illustrations. Price 45*s.* net.

This monograph gives an account of a valuable piece of clinical research carried out by its author as a radiologist under the active service conditions of a temporary base hospital. It is a very readable and well-produced book which reflects great credit on both the author and his publishers. Compared with a work of art, the book may be called " impressionist ". It is not any the worse for that. It is often a good thing to cut adrift from academic points of view. The title of the book is perhaps a little misleading, for the whole subject of low back structural derangement is not dealt with exhaustively. Instead we find a discussion mainly on the defects in the posterior neural arches in the lumbar region. A very brief introductory chapter discusses defective ossification of the *pars interarticularis*, and it is really discussion of this type of lesion which is the main theme of the book. The first chapter is followed by critical notes upon sixty-four cases, comprising cases of spondylolisthesis, bilateral spondylolysis, unilateral spondylolysis, defects of ossification in the articular processes, etc. A large series of radiological studies follows, and, finally, seven small chapters giving a detailed exposition of the author's main thesis. Roberts brings out the well-known fact that at least 5 per cent. of normal individuals appear to have defects of ossification of the *pars interarticularis*. He regards these defects as reactions to stress during the plastic period of growth. His view is that these deformities are not in themselves the cause of all the symptoms, but that they indicate a structural defect which must be counteracted by the soft tissues, and the latter therefore are more susceptible to any overstrain which may occur. Having come to the conclusion that trauma was only an incidental aggravating factor, the author carried out an exhaustive inquiry into the clinical background and life histories of each of his patients. Important points were gathered which would have been missed in the course of routine army consultations. We are led to the conclusion that initial trauma is followed by damage to the muscular and ligamentous apparatus with oedema in the overstrained soft tissues, as discussed by Lewis and Kellgren. The tragic story is repeatedly told of men suffering from structural low back derangement with these associated neurovascular disturbances, often with related visceral symptoms, whose organic lesions have been neglected on account of psychiatric concentration upon psychosomatic disorders. The trouble with chronic low backache is that an anxiety state is frequently an added factor due to the incompetence of medical men—their failure to take adequate clinical histories, failure to take an all round view of the case, and failure, through ignorance, to arrive accurately at the underlying structural defects. The author concludes by stating that there is a strong case for reconsideration of the attitude to these patients who suffer from " our inability to comprehend the underlying pathological changes, before they join the swelling ranks of so-called psychosomatic disorders ".

It is difficult to do justice in a brief review to all that Dr. Roberts brings out. He would probably be the first to recognize that he was working under abnormal conditions, and that he is emphasizing only one facet of the structural problem of backache. We have perhaps heard too much in the recent past about psychosomatic disorders and about intervertebral disc retropulsion. Let us recognize that there are other important pathological defects. Dr. Roberts's restrained style is so readable that one readily forgives the defects, which are few and unimportant. He overlooks much recent British writing upon the subject that he is discussing, and it is a pity to refer so often to a patient just as a " chronic backache ". He does immense good in pulling the legs of the gynaecologists, neurologists, abdominal surgeons, internists, and psychiatrists, particularly the latter. NORMAN CAPENER.

Rheumatism and Soft Tissue Injuries. By James Cyriax, M.D. 1947. Hamish Hamilton. London. Pp. 410: 101 figures and 107 plates. Price 42*s.*

The bulk of this work is devoted to a careful and well-illustrated description of the author's methods of diagnosis of soft-tissue lesions by palpation, by active and passive movements, and by use of local anaesthetic. The localization of soft-tissue injuries is covered region by region and is clearly and carefully presented; those who have to deal with this difficult subject will learn much by studying the author's methods. Emphasis is laid not on the pathology but on localization, and importance is rightly given to Kellgren's work. Admittedly the pathology of many of these lesions is obscure, but the relegation of its significance to a minor place may not appeal to those brought up to believe that correct diagnosis and treatment depend on the elucidation of the pathological lesion.

Dr. Cyriax writes that " nodules have nothing to do with rheumatism or fibrositis ", but says they feel like fibro-lipomata, quite ignoring the fact that in 1944 Copeman and Ackerman showed that some were in fact herniated lobules of fat.

Many will agree with the author's belief that treatment by rest may be wrong when applied to traumatic inflammation and in fact may lead to chronic disability. Scarring as a result of trauma is said to play a major part in the syndrome of fibrositis, and the value of deep massage in the treatment of soft tissue scars is stressed. Modern thought is followed in the chapter on perineuritis, where it is stated that a primary neuritis does not occur and that the lesion is due to outside pressure on the nerve.

The diagnosis of backache is dealt with at length, and prominence is rightly given to the prolapsed intervertebral disc, but little reference is made to other lesions of the osseous system or to those of the renal and gynaecological systems, which are so important in the differential diagnosis. For the treatment of the prolapsed disc the author advocates manipulation, epidural injection, and operation in that order, but perhaps does not give due credit to spinal immobilization, which is successful in many cases. In spondylitis deformans

forced movement is recommended, but it is not sufficiently stressed that if this is done in the active stage of the disease there may be a very painful reaction.

The large subject of rheumatoid arthritis is dealt with in a few pages. Gold salt therapy is suggested and the toxic manifestations are mentioned, but no advice is given as to their treatment. Osteo-arthritis is dealt with in an even more summary manner.

It is difficult to understand why the author of this well-produced book has included the term rheumatism in his title, for he dismisses most types of the rheumatic diseases briefly at the beginning and end of the book.

OSWALD SAVAGE.

The Treatment of Rheumatism in General Practice. By W. S. C. Copeman. Fourth Edition. 1947. Edward Arnold. London. Pp. 258. Price 12*s*. 6*d*.

The publication of a fourth edition of a scientific work is sufficient guarantee that it has been approved by the profession, and Dr. Copeman's book is no exception. The book has been brought up to date by alterations and additions, including the work of Copeman and Ackerman on the painful fibrositic nodule and the author's experience of infective neuritis during his war service.

There are certain refinements which might be made in future editions. The tendency to repeat descriptions and details of treatment is noticeable, and, as pentothal anaesthesia is no longer a novelty, the detailed account of its administration could be omitted.

In the chapter on sciatica, the congenital deformity in the lumbo-sacral region described by Professor Putti is mentioned. When this condition was first noticed, it was considered to be the cause of certain cases of sciatica, but this claim has not been substantiated by experience. If it were considered advisable to mention the condition at all, it would seem to be more appropriate to place it in the section on lumbago in the chapter on fibrositis. The abnormality is noted most frequently in those patients over 40 years of age who are employed in heavy manual work and complain of low back pain.

In the chapter on gout, Harrogate is not mentioned as being a suitable Spa for the treatment of this disease, but Aix-les-Bains is mentioned. The waters of these two spas are very similar, and even the very mild magnesia water at Harrogate can be shown to stimulate the excretion of uric acid by as much as 30 per cent. when compared with plain water.

These are criticisms of minor details and only tend to accentuate the value of the book as a whole. There is no doubt that it should be read and remembered by every general practitioner in this country. If they followed this advice they would find that the treatment of rheumatism need not be a depressing process for the harassed doctor, but rather an interesting excursion into the realms of therapeutics.

W. YEOMAN.

APPOINTMENTS

Dr. J. H. Kellgren has been appointed Clinical Director of the Research Centre for Chronic Rheumatism at the University of Manchester.

Dr. Kellgren qualified M.B., B.S., in 1934 and gained the M.R.C.P. in 1935 and the F.R.C.S. the following year. After this he spent three years with Sir Thomas Lewis, doing experimental work on pain localization, and taking part in the clinical activities of the Department of Clinical Research at University College Hospital. During this period he gained special experience in the rheumatic field by working in the physiotherapy departments of St. Thomas's Hospital.

He spent the war in the R.A.M.C. as a surgical and orthopaedic specialist in the Mediterranean. On demobilization he was appointed to the scientific staff of the Medical Research Council, and up to the time of his present appointment was working at the Wingfield-Morris Hospital, Oxford.

Throughout his work Dr. Kellgren has combined clinical with experimental activities, and his published works include papers on the localization and behaviour of deep pain sensibility and the applications of this work to the clinical problems such as abdominal pain, sciatica, causalgia, and osteo-arthritis.

Dr. G. Norman Myers has been appointed to the newly instituted post of Director of Research in Rheumatism at the University of Leeds. Dr. Myers was awarded a Beit Fellowship in 1930, and later became a research fellow and demonstrator in pharmacology at Cambridge University. He has examined for the university in pharmacology and therapeutics and has been consulting physician in aero-research at Duxford. In 1931 he revised the second edition of Cow's "Synopsis of Pharmacology", and other publications included papers on the influence of emulsions of oil upon the lethal effects of bacterial toxins, the effects of morphine upon the alimentary canal, and the pharmacological action of nikethamide.

ANNUAL MEETING OF THE INTERNATIONAL SOCIETY OF MEDICAL HYDROLOGY

The twenty-fifth annual meeting of the Society was held in Rheinfelden, Switzerland, from Sept. 10 to 14. Members representing nine countries were present.

At a council meeting held before the congress Dr. Barnes Burt (Bath) was elected Chairman of the Council. The Vice-Chairman were Prof. Frantistek Lenoch (Prague), Dr. G. D. Kersley (Bath), Prof. Walthard (Geneva); the Treasurer Dr. F. Clayton (Leamington), and the Secretary Dr. Donald Wilson (Bath).

This meeting coincided with the twenty-fifth anniversary of the Society, and it was unanimously agreed that in spite of the many difficulties this Society still played a useful part in the international recognition of balneotherapy.

OBITUARIES

The pressure on space in the last two issues of 1947 was so great that we were unable to publish an appreciation of Professor Sven Ingvar, who died early last year. We are indebted to Professor Nanna Svartz for the following appreciation.

Sven Ingvar, Professor of Internal Medicine in Lund, Sweden, died on April 21, 1947. He was born in 1889. Since 1929 he was head of the department of Internal Medicine at the University of Lund, to which was attached a rheumatism section with seventy beds. Ingvar's scientific work was chiefly in neurology, especially the pathology of the cerebellum and the reflex of the pupil; but he was also very interested in rheumatology, and visited the Fourth International Congress of Rheumatology in 1934 and was President of the Fifth International Congress in Sweden in 1936. On this occasion, as well as at other conferences, he often talked about the future of rheumatology and emphasized its close relation to the whole of internal medicine. He laid stress upon the importance of research work for the progress of this specialty, and stimulated his pupils to investigations in this field.

Soon after having celebrated his sixtieth birthday with his friends and pupils, Professor K. von Neergaard died on November 7 last, quite unexpectedly torn from his unceasing activity.

After a sound training under the recently deceased Prof. R. Staehelin, of Basle, von Neergaard, in 1925, began his career as head physician of the University-Institute of Physical Medicine at Zürich. In 1935, he became a titulary Professor, and in 1940 extraordinary Professor for Physical Medicine. The results of analytical research could, however, not satisfy one of his universal learning, which did not stop with studies on medicine and natural science; he felt he must search after a far-reaching synthesis. The result of this research is shown in his monograph on *Die Katarrhinfektion als chronische Allgemeinerkrankung, eine dynamische Reaktionspathologie des Rheumatismus und aetiologisch zugehöriger Erkrankungen, als Ausdruck einer spezifishen Virusinfektion.* He was one of the first rheumatologists to point out the importance of chronic infection and related allergic symptoms, and he was thus able to correlate the various forms of rheumatism into a unity. To him, the multiplicity of the rheumatic diseases was an expression of general illness. He therefore laid great stress on such general treatment as climato-therapy, balneotherapy, and physical-therapeutic unspecific influence, but without neglecting local therapy. After having dealt with the problem of local and general treatment, he wrote: " There is no question of ' either—or ', the only way is, carefully to consider in each individual case the ' this ', as well as the ' other '. Here, the great problem of our time—which is not only the biggest and most urgent in biology and medicine—the question of the relation of the particle to the whole, and the whole to the particle, finds an answer for a large group of diseases, at least in their fundamental basis."

Von Neergaard, moreover, was not content simply with scientific knowledge. He gave his whole life to the sick. For him it was not only the disease that was interesting, but the sick person himself. Without thorough social measures, such as sanitation of dwellings and factories, the establishment of public treatment at spas and resorts in the Swiss high mountains, without treatment of the pre-morbid state, without prophylactic measures of various kinds, the fight against the most frequent disease in Switzerland was impossible. This prompted him to work out a very detailed health programme for Switzerland, and also to further with all his energy the European League against Rheumatism. Unfortunately illness made it impossible for him to attend the first Congress of this League at Copenhagen. It remains for us to follow in the ways he showed us, by giving effect as far as possible to his really grand programme. In this way, too, we can fulfil his sincere wish for universal co-operation between the representatives of medical and other sciences, and, perhaps, ultimately contribute to the world's peace. A. BÖNI.